PARKINSON'S DISEASE, COGNITIVE STATUS AND CAREGIVER OUTCOMES.

A thesis submitted in partial fulfilment of the requirements for the degree of

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ABSTRACT

Cognitive impairment in Parkinson's disease (PD) can impact negatively on caregivers and is associated with carer distress and feelings of burden. To investigate this relationship we examined level of burden, coping strategies, depression, anxiety and potential positive aspects of caregiving in the caregivers of 104 PD patients. The PD patients were classified as either showing normal cognition (PD-N; n=57), with mild cognitive impairment (PD-MCI; n=31) or with dementia (PD-D; n=16). The key finding was that mean Zarit burden score increased between carers of PD-N (M=14.1, SD=12.0) through to PD-MCI (M=21.1, SD=9.86) and PD-D (M=27.8, SD=10.61); F (2,101) =9.96, $p<0.001$. Post hoc tests (Newman-Keuls) identified significantly higher Zarit burden scores in PD-D caregivers compared to both PD-N ($p<.001$) and PD-MCI patients ($p<.05$), but carers of PD-MCI patients also showed increased burden scores relative to those of PD-N patients ($p<.05$). The proportion of carers showing significant levels of burden (Zarit burden score ≥21) also increased as cognition declined (21% for PD-N; 58% for PD-MCI; and 81% for PD-D). Time spent providing care and problem-focused, emotion-focused and dysfunctional coping strategies also increased with worsening cognition. While caregiver use of problem-focused coping mediated the association between patient cognitive status and caregiver burden, we could not be confident about this relationship as the inverse model was also significant. Caregiver Zarit burden was independent of caregiver depression, anxiety and positive attributions of caregiving. The study highlights the impact of Parkinson's disease on those providing care when the patients' cognition is poor, including those with MCI. Caregiver well-being has important implications for nursing home placement and disease course.

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1 INTRODUCTION.

Parkinson's disease (PD) is a motor disorder in which cognitive and behavioural sequelae are now better recognized as having a significant impact on patient well-being (Janvin, Aarsland, & Larsen, 2005). Cognitive decline in PD is also likely to impact on caregivers but this important facet of the disorder is less well documented. Recently, published criteria characterise PD cognition into 3 levels of cognitive status, those patients with relatively normal cognition (PD-N), those with mild cognitive impairment (PD-MCI) and those with dementia (PD-D) (Emre et al., 2007; Litvan et al., 2012). This new perspective underscores the need to investigate the influence of these different levels of cognitive status on caregiver outcome in PD. Dementia is expected to be associated with increased burden for caregivers of PD patients (Leroi, McDonald, Pantula, & Harbishettar, 2012; Thommessen et al., 2002), but mild cognitive impairment and neurobehavioural symptoms may also generate increased risk of negative outcomes for caregivers beyond that associated with the motor disorder that characterises PD.

The following section outlines current perspectives on cognition in PD. The subsequent section describes caregiving in general terms as well as in the PD context. An overview of other factors that influence outcomes for PD caregivers is then provided. The chapter concludes with a brief summary of the rationale for the current study.

1.1 Cognition in Parkinson's disease.

Parkinson's disease is a complex motor disorder that is clinically manifest when dopaminergic cell depletion in the substantia nigra leads to the cardinal motor symptoms of PD (Braak et al., 2003). Cognitive and behavioural symptoms in PD relate to deficiencies in serotonergic, noradrenergic and cholinergic neurotransmission, in addition to dopaminergic decline, and neuropathological changes across many brain systems (Braak et al., 2003; Jellinger, 2012). Symptomology is often variable and often unpredictable, although an influential perspective is that changes broadly often follow a predictable pattern (Beach et al., 2009; Braak et al., 2003). The unfolding complexity of this disease process makes PD caregiving uniquely challenging for patients and caregivers (Hooker, Manoogian-O'Dell, Monahan, Frazier, & Shifren, 2000).

Cognitive difficulties in PD may occur at varying stages of the disease. These deficits span any of the core cognitive domains of attention, visuospatial function, executive function and memory. Progressive worsening of cognitive function may eventually impact a patient's ability to carry out activities of daily living and thus result in dementia (Dubois et al., 2007). Age of PD onset, duration of disease, long term use of medication, severity of motor symptoms and a low prodromal level of cognitive functioning are often cited as risk factors for major cognitive decline (Bosboom, Stoffers, & Wolters, 2004). Dementia is common among patients with an average incidence of 30-40 % in cross-sectional studies (Emre et al., 2007) and a cumulative prevalence of 75%-90% (Hely, Reid, Adena, Halliday, & Morris, 2008). Thus cognitive decline is a factor that will impact nearly all PD patients and their carers.

With increased awareness of the high probability of future dementia is a growing interest in the identification and description of PD patients with mild cognitive impairment (PD-MCI), which carries an increased probability of future dementia (Pedersen, Larsen, Tysnes, & Alves, 2013). Until recently a description of PD-MCI has been lacking but has relevance to our understanding of the effect of cognitive decline. PD-MCI status may provide a well-characterized patient population for examining outcome measures for clinical trials and a useful clinical entity to enable patients, caregivers, clinicians and researchers to improve care and research efforts (Litvan et al., 2012).

Recently published guidelines by the Movement Disorders (MDS) Task Force describe inclusion/exclusion criteria for PD–MCI (Litvan et al., 2012). Two levels of assessment have been suggested depending on the need for clinical characterisation and diagnostic certainty. Both levels require cognitive decline in the context of established PD with impairments not interfering significantly with functional independence. Level I consists of a brief assessment demonstrating impairment on global cognitive tests or impairment on 1 or 2 tests in less than 5 different cognitive domains. The more comprehensive Level II assessment requires assessment of at least 2 tests within each of the 5 cognitive domains of attention and working memory, executive function, language, memory and visuospatial function. Impairment is required on at least 2 neuropsychological tests in 1 or 2 of these cognitive domains, although the level of impairment is not fixed and allowed to span

anywhere from 1 to 2 standard deviations below normative data, pending researchers' preferences and taking into account estimated levels of premorbid functioning.

Inclusion criteria for probable PD-D are the development of dementia within the context of established PD, shown by impairment in at least 2 cognitive domains that coexist with and are deemed responsible for impaired activities of daily living (ie. loss of functional independence not due to motor complications). The presence of at least one behavioural symptom supports the diagnosis of probable PD-D but a lack of behavioural symptoms does not exclude it. Possible PD-D differs from probable PD-D in that, atypical cognitive impairments are present with the co-existence of other abnormalities that may instead cause cognitive impairment. When the time interval between the development of motor symptoms and significant loss of everyday functional independence is unknown a diagnosis of possible PD-D is also preferable to probable PD-D unless a diagnosis of Dementia with Lewy Bodies is more likely (McKeith & Mosimann, 2004).

1.2 Caregiving in Parkinson's disease.

Ageing populations are creating an increased demand for health care services and an increase in the incidence of age-related neurodegenerative disorders (Cornwall & Davey, 2004). Along with the rise in caregiver numbers is an appreciation of the increased strain and distress that can accompany care provision. The term 'the hidden patient' was coined in 1979 to describe the spouses of disabled elderly men, to emphasize the negative impact of caregiving (Fengler & Goodrich, 1979). In New Zealand caregiving is common and saves the formal health care system millions of dollars annually. Caregivers are predominantly female and middle aged (Goodhead & McDonald, 2007). Influences on caregivers depend on the nature and stage of the illness or injury; progressive diseases such as PD may create escalating dependency and distress on caregivers. Caregiving research has become the focus of clinical studies to improve knowledge of the determinants of caregiver outcomes and as an outcome variable for the pharmaceutical industry to evaluate the effects of new drug therapies for patients (Carter, Stewart, Lyons, & Archbold, 2008; Goodhead & McDonald, 2007).

In the last two decades over 400 empirical studies on the psychological effects of caregiving have been published but few have investigated PD caregiving (Pinquart & Sorensen, 2003). The heterogeneous nature, prognosis, and progression of PD as well as the beneficial effect of interventions, underscore the need for factors leading to caregiver distress to be clearly identified and described. The wider caregiving literature has seen a recent trend to consider not only relevant patient and caregiver characteristics, but also the mechanisms determining outcomes (Pinquart & Sorensen, 2003). Additionally, the newly identified clinical entity of PD-MCI has relevance for caregivers, as problems appearing early have long-term implications for caregivers' outcomes such as burden and depression (Blieszner & Roberto, 2010). The characterisation of PD-MCI has been described as a "crucial and unmet need for the overall care of PD patients" (Litvan et al., 2012).

Parkinson's Disease Cognition and Caregiving.

To the best of our knowledge, 11 studies and one meta-analysis (Lau & Au, 2011) have investigated the impact of cognition on PD caregivers but the results were contradictory (Table 1-1). Six studies reported a significant relationship between PD patient cognitive status and negative caregiver outcome and 5 studies found no association. The meta-analysis reported a significant association between PD patient cognition and negative caregiver outcomes and this is discussed in detail later. The studies included in the meta-analysis are indicated in Table 1-1.

Some investigators used only mental status tests. Three studies found a significant association between the Mini-Mental State Exam (MMSE) and negative caregiver outcome (Aarsland, Larsen, Karlsen, Lim, & Tandberg, 1999; Cifu et al., 2006; Martinez-Martin et al., 2008; Thommessen et al., 2002) while two studies found no association (D'Amelio et al., 2009; Fernandez, Tabamo, David, & Friedman, 2001). However the MMSE is only a screening instrument (Nasreddine et al., 2005) and its use has led to some debate because of floor and ceiling effects which may fail to identify patients with early dementia (Nieuwenhuis-Mark, 2010). Others employed instruments to identify impairment across cognitive domains although in the main these were limited to tests in 1 or 2 domains (Carter, Stewart, Lyons, & Archbold, 2008; Miller, Berrios, & Politynska, 1996). The current Movement Disorders Society Task Force guidelines require more thorough assessment to establish cognitive

status and highlight the importance of PD-MCI as a clinical entity (Litvan et al., 2012). Dementia ratings were provided in two studies; one reported that there was no association between Dementia Rating Scale (DRS) score and Zarit burden (Cifu et al., 2006) and in the other dementia status was associated with but not predictive of caregiver stress (Aarsland, Larsen, Karlsen, Lim, & Tandberg, 1999). In terms of describing caregiver outcomes, the Zarit Burden Interview (ZBI) remains the most widely used instrument in the general caregiving literature, but this instrument has been used infrequently in PD caregiving studies (Table 1-1). All three studies using the ZBI reported significant associations with cognitive impairment (Cifu et al., 2006; Leroi, McDonald, Pantula, & Harbishettar, 2012; Martinez-Martin et al., 2008).

The significant but complex relationship between PD patient cognitive status and negative caregiver outcomes has been highlighted in several studies. Aarsland et al. (1999) and Martinez-Martin et al. (2007) investigated the impact of patient cognition, neuropsychiatric and motor symptoms on caregivers and found significant associations between these variables and negative caregiver outcomes. Only the study by Aarsland et al. (1999) included PD-D patients. Both investigations reported that cognitive impairment and neuropsychiatric symptoms were the strongest predictors of negative caregiver outcome (Table 1-1). The multiple regression techniques employed in these studies highlight that while cognition is an important factor, neuropsychiatric symptoms are also noteworthy. Carter and colleagues (2008) used caregiver depression as the outcome variable in multiple regression and found that while motor symptoms made a modest contribution, PD patients' abilities in delayed recall was the strongest predictor in the model. Thommessen and colleagues (2002) compared outcomes for caregivers of dementia, stroke and PD patients (none of whom had PD-D). It was reported that cognition and depression were the strongest predictors of psychosocial burden in all 3 groups. The authors also found that mean Mini Mental State Exam (MMSE) scores for the non-PD dementia patients were significantly lower than PD patients but that PD caregivers experienced more burden. This finding highlights the increased burden among PD caregivers in addition to cognition.

Table 1-1. Studies including PD patient cognition in determinants of caregiver outcome.

Authors	PD Patient Cog Status	PD patient assessment tools	Measures of CG distress	Correlates/Predictors of negative outcomes for caregivers
*Aarsland et al., 1999 (n=94)	20 PD-D	MMSE, UPDRS-II and III, S&E, DRS, H&Y, ADL, NPI, MADRS, BDI	RSS, BDI, GHQ	Cognitive impairment and neuropsychiatric symptoms predicted CG poor health Cognitive impairment and patient depression predicted CG social distress Patient depression and neuropsychiatric symptoms predicted CG depression
*Carter et al., 2008 (n=219)	Not given (Early or middle stage)	Delayed recall; UPDRS –III & ADL, , HDRS	Family Care Inventory, CES-D	Cognitive impairment Depression
*Cifu et al., 2006 (n=49)	Not given (Only 80% with PD)	MMSE, DRS-2, UPDRS I-IV,Pain VAS, H&Y, S&E ADL	ZBI, Caregiver survey CDS (NPI)	Cognitive impairment, sleep problems, difficulties with activities of daily living and motor symptoms
D'Amelio et al., 2009 (n=)=40	5 PD-D	MMSE, UPDRS II and III H&Y, NPI, GDS	CBI and GDS	PD patient disease severity Neuropsychiatric symptoms
*Fernandez 2001 (n=45)	MMSE range = 13-30	MMSE, Neuropsychiatric Qs. UPDRS-III, H&Y, HAMD-17,BDI-II	HAMD-17, BDI-II	Disease duration Patient depression
Lee et al., 2012 (n=32)	32 PD-D	CAMCOG, UPDRS II and III	NPI CG distress scale, DCFS	Cognitive fluctuations, subtype diagnosis, and neuropsychiatric symptoms
Leroi et al., 2012 (n=102)	n=54(PD-N) n=48(PD-MCI) n=25(PD-D)	NP tests* (MDS critera) PDQ-8, NPI, UPDRS-II, IV and ADL	ZBI, NPI CG distress scale	Cognitive status in PD-D patients only
Martinez-Martin et al., 2008 (n=286)	SCOPA-Cog range= 2-40	SCOPA-Cog, H&Y, Motor, Sleep, Aut, and PS, HADS, PPRS, CISI-PD,PPRS, CIRS-G, VAS, EuroQoL	ZBI, HADS, EuroQoL	Cognitive impairment Caregiver affective status
*Meara et al., 1999 (n=132)	No severe dementia	CAMCOG, GDS, Webster Rating Scale	GDS	Cognition (trend only) Disease severity
*Miller et al.,1996 (n=54)	No given (disease duration ≥2 years)	Word reading, BLO, word recall, Webster Scale, NWS, H&Y, KPSS, WHO Scale	GHQ, GDS, BDI, MSS	Patient depression Motor symptoms
Thommessen et al., 2002 (n=58)	Mean MMSE = 26.2	MMSE, MADRS, UPDRS-ADL	RSS	Cognition Patient depression

* Adapted from Lau & Au, 2011.

ABS Affect Balance Scale; ADL-IS Activities of Daily Living; BDI Beck Depression Inventory; BLO Benton Line Orientation test; CAMCOG Cambridge Cognitive Examination; CBI Caregiver Burden Inventory; CDS (NPI) Caregiver Distress Scale of Neuropsychiatric Inventory; CES-D Centre of Epidemiological Studies Depression scale; CIRS-G Cumulative Illness Rating Scale-Geriatrics; CSI Caregiver Strain Inventory; DCFS Dementia Cognitive Fluctuations Scale; DRS Dementia Rating Scale; EuroQoL European scale of Health-related Quality of Life; HADS Hospital Anxiety and Depression Scale; HAMD-17 Hamilton Depression Scale; HDRS Hamilton Depression Rating Scale; H&Y Hoehn & Yahr; GDS Geriatric Depression Scale; GHQ General Health Questionnaire; ISAPD-ADL Intermediate Scale for Assessment of Parkinson's disease; KPSS Karnofsky Performance Status Scale; MADRS Montgomery-Asberg Depression Rating Scale; MMSE Mini-Mental State Exam;MSS Machin Strain Scale; NPI Neuropsychiatric Inventory; NWS North Western Scale; PDQ Patient Functional Status; PPRS Parkinson's disease Psychosis Rating Scale; RDRS-2 Rapid Disability Rating Scale. RSS Relatives' Stress Scale; SCOPA-Cog, motor, sleep, Aut and PS Scales for outcomes in Parkinson's disease-Cognition, motor , sleep, Autonomic, Psychosocial; S&E ADL Swab & England Activities of Daily Living; SF-12v2 Short Form Health Survey version 2; SF-36 Short Form Health Survey; SOC Sense of Coherence; SQLC Scale of Quality of Life of Caregivers; SSSQ Short Social Support Questionnaire; UPDRS-ADL Unified Parkinson's Disease Rating Scale-Activities of Daily Living; UPDRS Unified Parkinson's Disease Rating Scale Parts I-IV; VAS visual analogue scale for pain; Webster Rating Scale; WHO scale Measure of disability; ZBI Zarit Burden Interview; *NP Neuropsychological testing following Movement Disorders guidelines, level I criteria.

The study by Leroi and colleagues (2012) is the only study that has reported on the impact of PD-N, PD-MCI and PD-D on caregiver burden since the Movement Disorders Society (MDS) Task Force guidelines were published. Correlation analyses for the entire group revealed significant associations between motor severity, duration of motor symptoms and Mini-Mental State Exam score with caregiver burden. The authors found that caregiver burden was similar in those caring for patients without dementia (PD-N and PD-MCI) but significantly greater for those caring for patients with PD-D. The results were similar for PD patient quality of life measures with similar scores in those caring for patients without dementia (PD-N and PD-MCI) but significantly less for those caring for patients with PD-D. In terms of patient neuropsychiatric symptoms, no significant differences between the three groups were found. Leroi and colleagues (2012) established cognitive status with level I criteria which including eight neuropsychological tests in attention and working memory, executive function, memory and visuo-spatial function as well as the Mini-Mental State Exam (MMSE). In brief, PD-MCI was identified in patients with a MMSE score ≥ 26, cognitive deficits on at least two of the eight tests with deficits defined as at least 1.5 standard deviations below norms and cognitive deficits not severe enough to interfere with activities of daily living. PD-D status was established with MDS criteria, (Emre et al., 2007) including MMSE score < 26, deficits in more than one cognitive domain and functional impairment due to cognitive deficits. This neuropsychological assessment was insufficient to reach level II criteria and thus has less diagnostic certainty (Litvan et al., 2012) which may have led to some incorrect cognitive classification.

Several other PD caregiving studies have provided evidence that factors other than cognition are also associated with negative caregiver outcomes. Relative to the Mini-Mental State Exam, one study reported that disease stage and neuropsychiatric symptoms more strongly predicted burden (D'Amelio et al., 2009) and another that disease duration predicted caregiver depression (Fernandez, Tabamo, David, & Friedman, 2001). Miller and colleagues (1996) found that cognitive test scores correlated with caregiver depression but only patient depression and physical functioning predicted caregiver distress in multiple regression analyses. Another early study used a more detailed cognitive assessment instrument, the Cambridge Cognitive Examination (CAMCOG), but only a trend towards association

with caregiver depression was found (Meara, Mitchelmore, & Hobson, 1999). Lee and colleagues (2012) also used the CAMCOG to assess patient cognition when they compared outcomes for caregivers of patients with different types of dementia; Dementia with Lewy Bodies, Alzheimer's, vascular dementia and PD-D. The authors reported that type of dementia and cognitive fluctuation score were the significant predictors of caregiver stress.

The meta-analysis describing the correlates of caregiver distress in PD examined 10 studies (Lau & Au, 2011). It was concluded that motor symptoms had the strongest relationship with caregiver burden and depression. While the size of the associations were greater for motor symptoms (r=.42), there was also a significant correlation for cognition (r=.28). At the time of publication of the meta-analysis (2011) there were 9 studies with cognition as a factor available for inclusion however the authors only reported on 6 studies (Table 1-1). Hence the impact of PD patient cognition on caregiver outcome is not clear and requires further investigation.

In contrast to PD, the characterisation of MCI in Alzheimer's individuals is well-established (Petersen, 2004) and reports of MCI caregivers are emerging (Bruce, McQuiggan, Williams, Westervelt, & Tremont, 2008; Garand, Dew, Eazor, DeKosky, & Reynolds, 2005). One recent study (Bruce, McQuiggan, Williams, Westervelt, & Tremont, 2008) reported that 30% of Alzheimer's MCI caregivers demonstrated significant burden (Zarit burden score ≥ 21; Zarit, Reever, & Bach-Peterson, 1980). This study included use of a comprehensive neuropsychological battery to ensure that no patients met the criteria for a dementia diagnosis, and thus demonstrated the presence of caregiver burden in Alzheimer's MCI. An earlier smaller study (n = 27) of MCI patients reported that Alzheimer's caregivers had rates of distress that were intermediate to those of otherwise healthy older adults and those seen in dementia caregivers (Garand, Dew, Eazor, DeKosky, & Reynolds, 2005). It may be expected therefore, that PD-MCI would also be associated with caregiver burden.

Some researchers have excluded cognition from their investigations into PD caregiving and demonstrated that factors such as patient motor problems, neuropsychiatric symptoms and time spent caregiving also impact negatively on caregivers (Table 1-2). The results of these studies plus the

contradictory findings described in Table 1-1, suggest that cognition in combination with these other patient and caregiver variables may be associated with negative PD caregiver outcomes.

The Influence of PD Patient Motor Symptoms.

In their review of the treatment of behavioural symptoms and dementia in Parkinson's disease Hanagasi and Emre (2005) stated that these two symptoms are often more disabling than motor dysfunction. This view may hold for caregivers also although the results of studies investigating the impact of motor symptoms in PD are inconclusive (Table 1-1 and Table 1-2). In some studies significant associations between motor symptoms and negative caregiving outcomes became non-significant in multivariate analyses when cognitive and neurobehavioural symptoms are included, as described previously (Aarsland, Larsen, Karlsen, Lim, & Tandberg, 1999; Carter, Stewart, Lyons, & Archbold, 2008; Miller, Berrios, & Politynska, 1996). However a large study (n = 626) by Peters and colleagues (2011), used the Parkinson's Disease Questionnaire-39 (PD-Q-39) instrument which covers eight aspects of patient quality of life including cognition and concluded that patient limitations in physical mobility as well as caregiver problems with social support were strongly associated with caregiver strain. Schrag and colleagues (2006) also demonstrated a significant association between patient falls and caregiver burden although the incidence of falls and the presence of motor symptoms came from patient self-report which can be unreliable (MacKenzie, Byles, & D'Este, 2006).

Table 1-2. PD Caregiving studies not including patient cognition as a determinant of caregiver outcome.

Author/s	PD patient assessment tools	Measures of CG burden/distress	Significant associations with negative caregiver outcomes
Aarsland et al., 2007 (n=537)	UPDRS-III, NPI, H&Y	Distress scale of NPI	Delusions, apathy, aggression, depression and irritability
Caap-Ahlgren et al., 2001(n=67)	H&Y, Health PDQ-39	ZBI, SOC, GDS, social support	H&Y
Carter et al., 1998 (n=380)	H&Y	Family Caregiving Inventory	H&Y
Leiknes etal., 2010 (n=189)	NPI, UPDRS-ADL&III, H&Y	NPI distress scale	Apathy and depression H&Y
Martinez-Martin et al., 2007 (n=80)	SMS-ADL, H&Y, BI, CGI-S, HADS, EuroQOL, Hours spent caring	ZBI, HADS, SF-36, EuroQoL	H&Y, ADL BI, Scopa-II Mood HADS Hours of care
Peters et al., 2011 (n=626)	HealthSF-12v2, PDQ-39	SF-12v2 and CSI	PDQ-39 mobility, Social support

CGI-S Clinical Global Impression-Severity scale; EuroQoL European scale of Health-related Quality of Life; HADS Hospital Anxiety and Depression Scale; H&Y Hoehn & Yahr; GDS Geriatric Depression Scale; GHQ General Health Questionnaire; Health SF-12v2 Health Short Form 12 version 2; NPI Neuropsychiatric Inventory; NWS North Western Scale; PDQ-39 Patient Functional Status; SOC Sense of Coherence; UPDRS-ADL Unified Parkinson's Disease Rating Scale-Activities of Daily Living; UPDRS Unified Parkinson's Disease Rating Scale Parts I-IV; ZBI Zarit Burden Interview.

The Influence of Neuropsychiatric Symptoms in PD patients.

Various neurobehavioural symptoms are common in PD and are associated with caregiver distress (Aarsland et al., 2007; Lee, McKeith, Mosimann, Ghosh-Nodyal, & Thomas, 2012). The range of symptoms includes delusions, hallucinations, agitation/aggression, depression, anxiety, euphoria, apathy, disinhibition, irritability/lability, aberrant motor behaviour, sleep disturbances and appetite disturbances. They are usually quantified in terms of frequency and severity from caregiver reports; the Neuropsychiatric Inventory (NPI) is the most commonly used instrument for this purpose (Cummings et al., 1994). A large meta-analysis of 228 studies in the general caregiving literature reported that, of 6 caregiving-related variables (physical impairments, cognitive impairments, problem behaviour, hours of care, number of caregiving tasks and number of months in the caregiving role), care recipient's problem behaviour displayed the strongest association with caregiver burden and depression (Pinquart & Sorensen, 2003).

A large multicentre study provided a comprehensive description of the impact of neuropsychiatric symptoms in PD-D patients on caregiver distress (Aarsland et al., 2007) (Table 1-2).

Delusions, apathy, agitation, depression and irritability were associated with the highest distress scores, with moderate distress (Caregiver Distress Scale of the Neuropsychiatric Inventory ≥3; Cummings et al., 1994) reported by > 20% caregivers. Additionally, agitation was significantly associated with low Mini-Mental State Exam scores which reflects a relationship between neuropsychiatric symptoms and cognition.

Even newly diagnosed PD is associated with caregiver distress. One study compared Neuropsychiatric Inventory caregiver distress scores with those from a control group comprised of healthy individuals and their next of kin who provided information regarding patient's/control's neurobehaviour (Leiknes, Tysnes, Aarsland, & Larsen, 2010). Nearly 50% of the PD caregivers reported distress and more than 25% reported moderate distress (Caregiver Distress Scale of the Neuropsychiatric Inventory ≥3). Next of kin of patients with PD reported 3 times more burden in association with neuropsychiatric symptoms than those in the control group. Symptoms of apathy, depression, anxiety and irritability symptoms being the most troublesome.

Caregiver Depression and Anxiety.

Depression and anxiety measures in caregivers have been frequently used in caregiving studies as proxy markers for distress (Lee, McKeith, Mosimann, Ghosh-Nodyal, & Thomas, 2012; Pinquart & Sorensen, 2003). Most research examining depression in caregivers has focused on symptoms such as sadness or lack of energy rather than a diagnosis of clinical depression and has therefore used screening instruments as assessment tools (Table 1-1and Table 1-2). Several studies have demonstrated that PD patient variables such as disease severity, health status and mood disorder are associated with caregiver depression (Caap-Ahlgren & Dehlin, 2002; Carter et al., 1998; Fernandez, Tabamo, David, & Friedman, 2001). Others have reported that patient depression itself is associated with caregiver depression (Aarsland, Larsen, Karlsen, Lim, & Tandberg, 1999; Meara, Mitchelmore, & Hobson, 1999). Meara and colleagues (1999) also reported that 64% of PD patients and 34% of caregivers scored within the depressed range on the Geriatric Depression Scale-15 (≥5; Weintraub, Oehlberg, Katz, & Stern, 2006). Other investigators have provided caregiver rates as high as 54% (Caap-Ahlgren & Dehlin, 2002) and as low as 9.1% (Martinez-Martin et al., 2008). The general

caregiving literature has provided caregiver depression rates of between 12.5% and 24% (Livingston, Manela, & Katona, 1996; Molyneux, McCarthy, McEniff, Cryan, & Conroy, 2008) and one Alzheimer's disease study reported a 12.5% incidence of depression among mild cognitive impairment caregivers (Blieszner & Roberto, 2010).

Anxiety is less frequently reported in the PD caregiving literature although it is often co-morbid with depression (Andreescu et al., 2007). One group found that anxiety was significantly associated with Zarit burden, although in multiple regression anxiety did not feature in the model (Martinez-Martin et al., 2007) (Table 1-2). In a subsequent study Martinez-Martin and colleagues (2008) demonstrated that caregiver anxiety was related to disease severity, duration of care, costs and female gender, with 21.7% of caregivers and 25% of patients experiencing anxiety. Generally higher rates of anxiety (25%-57%) have been reported in the general caregiving literature (Cooper, Balamurali, & Livingston, 2007; Crespo, Lopez, & Zarit, 2005; Mahoney, Regan, Katona, & Livingston, 2005).

1.3 Additional Factors Influencing PD Caregivers.

Coping.

While the main aim of the current study was to examine the influence of PD patient cognitive status on caregiver outcome, a secondary aim was to investigate the possible mediating effect of other factors on this relationship. The value of this addition is that the construct of coping has been used in related research such as Alzheimer's disease, to explain variability in caregiver outcomes (Cooper, Katona, Orrell, & Livingston, 2008; Fillion, Kovacs, Gagnon, & Endler, 2003; Snell, Siegert, Hay-Smith, & Surgenor, 2011) and offers a focus for interventions (Pinquart & Sorensen, 2003; Sanders-Dewey, Mullins, & Chaney, 2001). Several theories of coping exist based on the early work of Lazarus and Folkman (1985) who conceptualized coping as an evaluation of a stressor, that shapes an individual's emotional and behavioural reactions (Maes, Leventhal, &De Ridder, 1996). According to Lazarus (1993) coping is a process that changes over time and situation rather than a trait. This approach is appropriate in a study of PD caregivers in which the variables of interest relate to how caregivers cope with different levels of patient cognitive impairment.

Folkman and Lazarus (1986) derived two theory-based dimensions of coping, problem-focused and emotional-focused coping. A third dimension, dysfunctional coping, was added by Carver, Scheier and Weintraub (1989). Problem-focused coping relates to trying to manage distress through confronting and altering the situation and includes strategies such taking action to improve the situation, seeking social support and planning. Use of this strategy may however be maladaptive for caregivers dealing with a progressive neurological disease such as PD. When a threat is appraised as uncontrollable, emotional-focused coping strategies are elicited. Emotional –focused coping concerns attempts to reduce distress by regulating emotions and includes strategies such as using humour, finding support through religion, positive reframing and acceptance. Thus emotion-focused coping may prove more adaptive than problem-focused coping strategies in the context of PD in which attempts to change the situation could create frustration and disappointment. While debate remains over the merits and disadvantages of problem-focused and emotion-focused strategies, theorists agree that dysfunctional strategies are invariably associated with more negative outcomes; they include substance use, behavioural disengagement and self-distraction (Austenfeld & Stanton, 2004).

One of 2 studies to examine coping in PD caregivers used the Revised Ways of Coping Checklist (WOCL), which includes only the problem-focused and emotion-focused dimensions of coping (Sanders-Dewey, Mullins, & Chaney, 2001). The authors reported that emotion-focused coping was found to be a significant predictor of caregiver distress in that more emotion-focused coping was associated with more distress. However in the WOCL instrument the emotion-focused dimension contains items of escape avoidance and distancing that are more similar to strategies described in other instruments as dysfunctional (Del-Pino-Casado, Frias-Osuna, Palomino-Moral, & Pancorbo-Hidalgo, 2011). The second study that explored coping in PD caregiving used the Sense of Coherence Scale (SOC), which captures global states of coping rather than strategies (Caap-Ahlgren & Dehlin, 2002). The authors reported that low sense of coherence (coping) was a significant predictor of caregiver burden in that when caregivers felt they were not coping they experienced more burden.

One longitudinal Alzheimer's study found that emotion-focused coping protected caregivers from developing anxiety a year later (Cooper, Katona, Orrell, & Livingston, 2008) whereas 2 other

dementia caregiving studies provided evidence of increased caregiver burden with the use of emotion-focused coping (Chou, LaMontagne, & Hepworth, 1999; Kramer, 1997). The evidence surrounding the adaptive or maladaptive potential of problem-focused coping in the general caregiving literature is also inconclusive (Chou, LaMontagne, & Hepworth, 1999; Montoro-Rodriguez & Gallagher-Thompson, 2009). In an effort to look beyond the associations between variables, Cooper and colleagues (2008) also examined coping using mediation analyses. Those authors reported that coping itself mediated the consequences of burden while others have found that coping strategies mediate the relationship between patient characteristics and caregiver outcomes (Cooper, Katona, Orrell, & Livingston, 2008; Kim, Knight, & Longmire, 2007; Tuokko, Kristjansson, & Miller, 1995). Further investigation into the direction of these relationships is required (de Pal Casado).

Positive Attributions of Caregiving.

Caregiving can be difficult and is associated with many negative outcomes, but some Alzheimer's caregivers report positivity towards their role (Tarlow et al., 2004). This perspective has not been applied in the PD context previously but offers an opportunity to expand current knowledge of the mechanisms determining outcomes (Pinquart & Sorensen, 2003). Tarlow and colleagues (2004) developed the Positive Attributions of Caregiving (PAC) to identify the positive aspects of caregiving in the dementia context although the instrument has yet to gain popularity. The instrument has been derived from the stress process model by Folkman (1986) where positive emotional outcomes facilitate continued coping which in turn reduces negative outcomes. This construct may have application in PD and act as a mediator between patient cognitive status and caregiver burden or as a factor related to coping. One large longitudinal study (n=243) found that low scores on PAC predicted AD caregiver burden and that PAC was negatively associated with caregiver depression (Hilgeman, Allen, DeCoster, & Burgio, 2007). In addition, AD caregivers who endorsed less PAC benefitted most from an intervention, consisting of a caregiver skill building programme, included in the study as an outcome variable.

Time Spent Caregiving.

In addition to the caregiver and patient variables described above, time devoted to PD caregiving has also been linked to negative caregiver outcomes. Several studies have found higher distress among caregivers who spend more time per week providing assistance in everyday tasks (Happe & Berger, 2002; Martinez-Martin et al., 2007; Schrag, Hovris, Morley, Quinn, & Jahanshahi, 2006). In another example of some of the inconsistences in the PD caregiving literature, a second study found there was no link between length of caregiving, when measured in years, and caregiver stress (McRae, Sherry, & Roper, 1999).

1.4 Rationale for the Current Study

The impact of cognition in PD on caregiver well-being is poorly documented. There are some reports of negative caregiver outcome in PD-D but none in PD-MCI. In the main the results of studies examining PD cognition in caregiving are conflicting. Recently published criteria characterise PD cognition into 3 levels of cognitive status, those patients with relatively normal cognition (PD-N), with mild cognitive impairment (PD-MCI) and with dementia (PD-D) (Litvan et al., 2012). While dementia can be expected to be associated with increased caregiver burden (Leroi, McDonald, Pantula, & Harbishettar, 2012; Thommessen et al., 2002), mild cognitive impairment and neurobehavioural symptoms may also generate increased risk of negative caregiver outcomes beyond that associated with the motor disorder that characterises PD. Hence this new perspective on PD patient cognitive status provides an opportunity to help clarify the influence of patient cognition on caregiver outcome.

After the current study commenced, one study published evidence on the impact of PD-N, PD-MCI and PD-D on caregivers (Leroi, McDonald, Pantula, & Harbishettar, 2012). The authors used a brief assessment battery of eight neuropsychological tests plus the Mini-Mental State Exam to classify PD patients according to level I Movement Disorders Society criteria (Litvan et al., 2012). As stated earlier, these authors reported significant Zarit burden differences between PD-N versus PD-D and PD-MCI versus PD-D, but not between PD-N versus PD-MCI. It was suggested that PD-MCI by definition would not include patients with functional impairment and therefore Zarit burden in this group would not be expected to differ significantly from those without any identified cognitive

impairment. However this premise requires further elucidation as it conflicts with the findings from Alzheimer's caregiving studies (Bruce, McQuiggan, Williams, Westervelt, & Tremont, 2008; Garand, Dew, Eazor, DeKosky, & Reynolds, 2005) and also suggests that caregiver burden is independent of patient cognition and more related to patient functional impairment. A more comprehensive neuropsychological assessment may provide improved diagnostic certainty regarding cognitive classification and generate increased confidence in any associations between patient cognitive status and caregiver burden.

The current study also further extended the work of Leroi and colleagues (2012) by investigating the possible mediating effects of caregivers coping strategies, positive attributions of caregiving and PD patients' neuropsychiatric symptoms between patient cognitive status and caregiver Zarit burden. Mediating variables provide an opportunity to look beyond observed associations and may suggest pointers for intervention. The construct of coping has not been well investigated in PD caregiving (Caap-Ahlgren & Dehlin, 2002; Sanders-Dewey, Mullins, & Chaney, 2001) and no studies have investigated the positive aspects of PD caregiving. Several previous PD caregiving studies have found that patient neuropsychiatric symptoms are associated with caregiver burden (Aarsland et al., 2007; Aarsland, Larsen, Karlsen, Lim, & Tandberg, 1999; Leiknes, Tysnes, Aarsland, & Larsen, 2010) and in at least one of these studies, cognitive status was also implicated (Aarsland et al., 2007).

In the current study, caregivers were also asked an open-ended question: "What is the hardest thing about providing care/support to someone with Parkinson's disease?" This additional qualitative question was added to complement the quantitative data obtained from the standardized questionnaires to allow potentially unasked issues to be raised.

2 METHOD

2.1 Overview

The current study employed a cross-sectional design to examine the influence of three levels of cognitive status in Parkinson's disease on their caregivers. Ethical approval for this investigation was given by the New Zealand Ministry of Health Upper South Island A Regional Ethics Committee (Reference URA/11/11/067) and all participants gave informed consent. Copies of the information sheets and consent forms given to Parkinson's disease patients and their significant others/caregivers are included in Appendix A.

2.2 Participants

One hundred and fifty five people who met the UK Parkinson's Disease Society's criteria for idiopathic Parkinson's disease (Hughes, Daniel, Kilford, & Lees, 1992) were identified through the database at the New Zealand Brain Research Institute (NZBRI) in Christchurch. Caregivers were identified as any person who was directly involved in the patient's care and provided some form of support with respect to everyday activities. In the caregiving literature terms such as caregiver, significant other and support person are used interchangeably. The caregiver did not need to be living with the PD patient and needed to complete self-assessment questionnaires. Only PD patients who had undertaken either detailed or brief cognitive assessment within 4 months of the caregiver interview were included. Of the 155 potential PD patients, 7 were unable to be contacted, 4 had died and 7 had no caregiver currently supporting them. A further 11 patients were about to undergo comprehensive neuropsychological assessment at the NZBRI for a separate study and were unable to undertake an additional study. Twenty two caregivers declined participating. A final sample of 104 patient-caregivers provided data for the current study: 74 women and 30 men. Sixty-five caregivers came to the NZBRI for interview and 39 caregivers were interviewed in their own homes. There were 91 spouses, 4 daughters, 4 sons, 1 brother, 1 daughter-in-law and 3 friend caregivers. Eighty nine caregivers lived with the person with PD; 15 caregivers lived at a separate address but spent a minimum of 4 hours a week caring for the PD patient.

Ninety eight percent of the PD patients identified themselves as being NZ European, 2% as Asian, none as Māori and none as Pacific Islanders, compared with Canterbury's 77% NZ European, 6% Asian and, 7% Māori and 2% Pacific Islander as provided by NZ's 2006 Census statistics information (Statistics New Zealand, Census 2006).

Classification of PD Patient Cognitive Status.

The patients were classified as showing normal cognition (PD-N), mild cognitive impairment (PD-MCI) or dementia (PD-D) (see Table 2-1 and Table 2-2 for assessments and Appendix B for further details). Sixty-seven PD patients had attended the NZBRI for detailed cognitive assessment relating to other studies within 4 months of the caregiver interview and these patients were classified by the assistant research fellow at the NZBRI (Lesley Livingston). Briefly, PD-D patients fulfilled the new diagnostic criteria of the Movement Disorders Society (Emre et al., 2007) as described in (Dalrymple-Alford et al., 2011; 2010). PD-MCI patients did not show significant impairment in everyday function and were required to show two deficits at 1.5SD below normative data within at least one cognitive domain. The remaining patients were classified as showing normal cognition (PD-N). The classification of these three distinct groups of patients has been further confirmed with neuroimaging (Dalrymple-Alford et al., 2011; Melzer et al., 2013) and while basic language measures did not form part of their evaluation, this cognitive domain does not generally distinguish these groups (Emre, 2007 and (Dalrymple-Alford et al., 2013).

A further 28 patients undertook an abbreviated neuropsychological assessment by the author (AJ) and were classified using 3 measures across 2 domains: Letter fluency, action fluency (executive function) and months reversed (working memory), as well as the Montreal Cognitive Assessment and the Mini-Mental State Exam. Cognitive status for these patients was also established by caregiver reports of patient abilities daily living tasks and neuropsychiatric symptoms. Receiver operating characteristic (ROC) curve analyses were used to evaluate cognition across the 5 "domains" within the Montreal Cognitive Assessment. For the brief assessment, PD patients were classified as PD-MCI if they demonstrated impairment on at least 2 tests in one or more domains but with no significant

impairments in activities of daily living (Litvan et al., 2012). ROC curve analyses, comparing the MoCA subtest scores between PD-N (n=38) and PD-MCI (n=24) in patients with full cognitive assessment were used to identify suitable cutoff criteria. Diagnostic values were determined with > 80% specificity [avoidance of true negatives] and 70-80% positive predictive values (PPV) [detection of an accurate positive test]. The optimal cutoff in MoCA items for *visuospatial function* was <4 (92% specificity, 77% PPV); for *working memory* < 2 (94% specificity, 78% PPV); for *attention* <5 (94% specificity, 78% PPV); for *language* <2 (specificity 97%, 67% PPV). The ROC curve comparisons of *semantic memory* and *orientation* were non-significant and were therefore excluded. A PD-D classification required a decline in everyday functional activities not attributed to motor impairment (ADL-IS; Reisberg, 2001), as demonstrated by scores on the mental status tests (<21 MoCA (Dalrymple-Alford et al., 2010) and a deficit in at least 2 cognitive domains (Emre, 2007).

Table 2-1 Individual PD patient neuropsychological test scores and domains (mean ± SD) n=67

	PD-N(n=38-57)	PD-MCI(n=24-31)	PD-D(n=5-16)	Analysis
Attention, Working memory and Processing Speed				
DigitsF/B	0.76 ± 0.9	0.12 ± 0.7	-0.14 ± 0.6	$F_{2,73}$=8.67, p<.001
Digit Ordering	-0.93 ± 0.9	-1.94 ± 0.5	-2.07 ± 0.8	$F_{2,73}$=15.74, p<.001
TEA (Map Search)	-0.41 ± 0.9	-1.43 ± 0.8	-1.69 ± 0.9	$F_{2,72}$=16.29, p<.001
Stroop colour	0.10 ± 0.8	-0.43 ± 1.1	-1.14 ± 1.2	$F_{2,73}$=8.82, p<.001
Stroop word	0.10 ± 0.9	-0.25 ± 0.9	-0.60 ± 1.1	$F_{2,73}$=22.94, p<.001
Trails A	0.32 ± 0.7	-0.20 ± 0.8	-1.52 ± 1.3	$F_{2,73}$=22.94, p<.001
Domain Score	0.01 ± 0.5	-0.69 ± 0.4	-1.18 ± 0.7	$F_{2,72}$=29.90, p<.001
Executive Function				
Letter Fluency[a]	0.54 ± 1.3	0.16 ± 1.4	-0.97 ± 0.8	$F_{2,73}$=3.55, p<.05
Action Fluency[a]	0.03 ± 1.0	-0.64 ± 1.0	-1.36 ± 0.9	$F_{2,73}$=9.76, p<.001
Category Fluency	0.75 ± 1.1	0.24 ± 0.9	-0.76 ± 1.2	$F_{2,73}$=9.87, p<.001
Category Switching	0.28 ± 1.3	-0.32 ± 1.1	-1.67 ± 1.2	$F_{2,73}$=13.45, p<.001
Trails B	0.26 ± 1.0	-0.25 ± 0.9	-1.96 ± 1.3	$F_{2,73}$=23.24, p<.001
Stroop	0.40 ± 0.9	-0.50 ± 1.2	-1.67 ± 1.2	$F_{2,73}$=18.94, p<.001
Domain Score	0.42 ± 0.8	-0.15 ± 0.7	-1.31 ± 0.9	$F_{2,72}$=29.90, p<.001
2.2.1.1 Visuoperceptual Visuospatial				
JOL	0.55 ± 0.6	-0.09 ± 0.9	0.02 ± 0.6	$F_{2,73}$=5.90, p<.01
Fragmented letters	0.82 ± 0.5	0.42 ± 0.8	0.27 ± 1.0	$F_{2,73}$=3.75, p<.05
Rey Copy	0.09 ± 1.0	-0.77 ± 1.3	-1.23 ± 1.4	$F_{2,73}$=7.92, p<.001
Domain Score	0.50 ± 0.4	-0.10 ± 0.6	-0.31 ± 0.7	$F_{2,72}$=29.90, p=.001
Learning & Memory				
CVLT Free recall	0.75 ± 1.1	-0.25 ± 0.9	-1.11 ± 1.2	$F_{2,73}$=17.10, p<.001
CVLT Short delay	0.57 ± 1.3	-0.27 ± 1.2	-1.29 ± 0.7	$F_{2,73}$=12.73, p<.001
CVLT Long delay	0.54 ± 0.9	-0.38 ± 1.0	-0.64 ± 0.5	$F_{2,73}$=11.57, p<.001
Rey Immediate	0.75 ± 1.5	-0.51 ± 1.3	-1.09 ± 1.0	$F_{2,72}$=11.61, p<.001
Rey Delayed	0.71 ± 1.7	-0.77 ± 1.3	-1.41 ± 1.3	$F_{2,70}$=11.63, p<.001
Domain Score	0.66 ± 1.2	-0.43 ± 0.8	-1.12 ± 0.7	$F_{2,72}$=29.90, p<.001
Global neuropsychological Z score	-0.91 ± 0.3	-0.39 ± 0.4	-0.91 ± 0.3	$F_{2,73}$=3.87, p<.05

PD-N, n=38; PD-MCI, n=24; PD-D, n=5, except [a]: PD-N, n= 57; PD-MCI, n= 31; PD-D, n=16 - these additions had abbreviated testing only whereas other non-dementia patients had detailed testing. PD-D patients received detailed testing and a confirmed diagnosis between 2 weeks and 4 years previously.
For details of tests see Appendix B

Table 2-2. Individual PD patient global cognitive assessment scores (mean ± SD) (n=104).

	PD-N(n=19-57)	PD-MCI(n=7-31)	PD-D(n=2-16)	Analysis
MoCA	26.59 ± 2.28	24.47± 2.49	20.65± 3.36	$F_{2,101}$ = 27.67, p<.001
MMSE	28.78 ± 1.41	27.37 ± 1.97	24.21 ± 3.11	$F_{2,101}$ = 32.869, p<.001
ADL-IS	0.58±0.59	0.63 ± 0.53	1.69 ±0.690	$F_{2,99}$ =23.073, p<.001
Months reversed[a]	18 P, 0 F	6 P, 2 F	1 P, 1 F	

PD-N, n=57; PD-MCI, n=31; PD-D, n=16, except [a]: PD-N, n= 19; PD-MCI, n= 7; PD-D, n=2 - only these patients did months reversed. PD-D patients received detailed testing and a confirmed diagnosis between 2 weeks and 4 years previously.
For details of tests see Appendix B

2.3 Caregiver Measures.

Caregivers were given 5 questionnaires concerning burden, coping strategies, positive attributions towards caregiving and personal depression and anxiety symptoms. Demographic information included the number of hours spent caregiving per week. In addition to the 5 questionnaires, caregivers who provided care for those PD patients who had not had detailed neuropsychological assessment within 4 months of the caregiver interview also completed instruments to assess the PD patient's everyday functional activities (Reisburg et al., 2001) and neuropsychiatric symptoms (Cummings et al., 1994).

Caregiver Measures: For PD Patients with Full and Brief Cognitive Assessment.

Burden.

The Zarit Burden Interview (Zarit, Reever, & Bach-Peterson, 1980) is the most widely used measure of caregiver burden (Ankri, Andrieu, Beaufils, Grand, & Henrard, 2005). Originally designed for use in the impaired elderly, the self-report measure has shown applicability in a variety of populations. Scores are unrelated to age, gender, living situation, locale, language, marital status or employment status. In dementia caregivers, the measure has good internal consistency reliability with a Cronbach's alpha of .92 (Hebert, Bravo, & Preville, 2000).

The ZBI (Appendix C-1) identifies the impact of the patient's disability on the caregiver/support person in terms of health, finances, social life and interpersonal relations. There are 22 items in the scale and participants were asked to choose the response that "best describes how they feel": never, rarely, sometimes, quite frequently or nearly always. The scores were summed with higher scores indicating greater caregiver/support person distress. Scores between 0 - 21 suggests no to mild burden; 21 - 40 = mild – moderate burden; 41 - 60 = moderate to severe burden; 61-88 = severe burden (Zarit, Reever, & Bach-Peterson, 1980).

Coping.

The brief Coping Orientations for Problems Experienced (COPE) assesses different coping strategies and is a shortened version of the 60 item COPE Inventory (Carver, 1997). The brief COPE (Appendix

C-2) omits 2 scales from the full COPE, adds one new scale and reduces the instrument from 4 to 2 items per scale. This self-report instrument has been used in health-related research including dementia caregivers (Cooper, Katona, Orrell, & Livingston, 2008; Crespo, Lopez, & Zarit, 2005). Carver (1997) suggests that the questionnaire can be modified to suit the research design and the wording adjusted depending on whether dispositional or situational coping is the construct of interest. The current study aimed to capture the caregiving experience at one point in time, therefore caregivers were asked to consider their current PD caregiving situation.

Responses were scored on a 4 point Likert scale ranging from 1 ("I haven't been doing this at all") to 4 ("I have been doing this a lot"). The brief COPE contains 28 items measuring 14 distinct coping reactions to stressful life events. Previously published literature has used 9, 3 and 2 factor solutions for the brief COPE (Carver, Scheier, & Weintraub, 1989; Cooper, Katona, Orrell, & Livingston, 2008; Snell, Siegert, Hay-Smith, & Surgenor). Principal components factor analysis on the current caregiver responses found a 3 factor solution, similar to that described by Cooper and colleagues (2008) in which items on the brief COPE formed clusters called problem-focused, emotion-focused and dysfunctional coping. The principal components factor analysis methodology used to derive the 3 factor solution is described in Appendix D. In brief, problem-focused coping included the subscale items: Active coping, seeking instrumental support, seeking emotional-support and planning; emotion-focused coping included: Religion, acceptance, humour and one item from the positive reframing subscale; dysfunctional coping included: Self-distraction, substance use, behavioural disengagement and venting.

Positive Attributions.

The Positive Aspects of Caregiving scale (PAC) is a 9-item measure designed for use in a range of caregiving environments to evaluate the positive dimensions of the caregiving experience (Tarlow et al., 2004). Each of the items begins with "Providing help to (name) has...." followed with specific items such as "Made me feel more useful" and "Enabled me to appreciate life more." Each item was rated on an ordinal scale ranging from 1 (*disagree a lot*) through to 5 (*agree a lot*). The items are

summed to give a total score for each participant. The reliability of the nine items was reported as high: Cronbach's alpha = 0.89 (Tarlow et al., 2004).

The PAC (Appendix C-3) was developed from previous work of Lawton and colleagues (1989, 1991). However the current PAC differed from this original measure in that: (1) items were changed from a yes/no format to increase variability of responses and improve reliability; (2) questions were rephrased as statements to allow response options; and (3) the instructions were simplified to aid administration.

Depression.

The 15-item Geriatric Depression Scale (GDS-15; Weintraub, Oehlberg, Katz, & Stern, 2006) is a screening instrument for depression in elderly populations (Appendix C-4). Participants were first presented with 4 questions relating to feelings of depression: eg. "Are you basically satisfied with your life?" If the caregiver agreed with any of these 4 statements another 11 statements were presented. For the GDS-15, 0-4=depression unlikely; 5-10= mild depression; > 10 are almost always depressed. The GDS has shown good internal consistency and validity in both elderly and younger populations (Rule, Harvery, & Dobbs, 2008).

Anxiety.

The geriatric anxiety inventory (GAI) is a 20-item self-report scale of agree/disagree statements which is able to discriminate between those with or without anxiety symptoms and those with and without DSMIV Generalized Anxiety Disorder (GAD). Participants were initially presented with 5 statements relating to feelings of anxiousness: eg. "I often feel nervous". If the caregiver agreed with 3 or more statements the further 15 statements were presented and a total score given: 0-1= anxiety unlikely; 2-8= mild anxiety; ≥9= possible anxiety disorder (Pachana et al., 2007). The instrument is provided in Appendix C-5.

"The Hardest Thing"

At the end of the interview caregivers were asked the single question, "What is the hardest thing about providing care/support to someone with PD?" When several difficult aspects of the role were provided the caregivers were encouraged to choose the *most* difficult of those options. These responses were recorded as falling into one of 8 categories: difficulties relating to personal or social interactions; nothing specifically relating to PD eg. "nothing in particular" or "I just don't love him any more"; physical symptomology of PD; worrying about the future; patient dependency; lack of time for oneself; whether to help the patient while they struggled to complete tasks; specific aspects of PD relating to individual caregivers eg. "The time taken to diagnose PD".

Premorbid IQ

Premorbid IQ of the caregivers was calculated based on occupation, years of education and age using the equation: 87.14 - (5.21 x occupation) + (1.78 x education) + (. 18 x age) to derive a full scale IQ (FSIQ) according to Crawford and colleagues (2001). Each participant's occupation was coded using the Office of Population Censuses and Surveys (1980). The Classification of Occupations consisted of five categories broadly defined as follows; 1 = professional, 2 = intermediate, 3 = skilled, 4 = semi-skilled, 5 = unskilled. Retired participants, and those describing themselves as househusbands/housewives, were coded by their previous occupations as were those currently unemployed. Those who had never worked were coded as 5 (i.e., unskilled).

Statistical analysis

One hundred four caregivers provided 95% power for a large effect size (f = 0.4). Analysis of variance, Chi square and t-tests were used to assess the relationships between demographic and clinical measures with caregiver outcome; multivariate analyses (linear, multiple regressions and path analyses) were employed to determine mediators of caregiver burden.

3 RESULTS

The demographic and clinical details for the PD patients and caregivers are shown in Table 3-1 and Table 3-2 respectively. The PD patients were aged between 48 to 82 years with 72% male and a mean educational level of 12.5 years; 98% identified themselves as New Zealand European (Table 3-1). Disease duration ranged from 1.5 to 31 years. Patients in the 3 cognitive status groups did not differ significantly in age, years of education, depression, anxiety or movement difficulties (UPDRS) (Table 3-1). Caregivers were aged between 23 and 83 years old, were predominantly a spouse (88%) and female (71%); their mean education duration was 12 years; 96% identified themselves as New Zealand European and 86% lived with the person with PD (Table 3-2). Caregivers of PD patients in the 3 cognitive status groups did not differ in age or years of education.

Table 3-1. Parkinson's disease patient demographic and clinical characteristics.

	PD-N	PD-MCI	PD-D	Analysis	Post Hoc
n	57	31	16		
Age	68.15 ± 8.1	70.23 ± 6.7	73.06 ± 4.8	$F_{2,101}$ =3.03, ns	
Female:Male	1:2.2	1:2.8	1:3		
Years Education	12.72 ± 2.6	12.37 ± 2.4	12.41 ± 2.7	$F_{2,101}$ <1.0	
Eth:NZer/Other*	56/1	30/1	16/0		
NPI[a]	3.43 ± 0.8	5.79 ± 0.9	9.85 ± 1.5	$F_{2, 91}$ = 10.12, p < 0.001	PD-N v PD-D p < .001; PD-MCI v PD-D p < .001
UPDRS[b]	23.89 ± 1.8	30.17 ± 2.9	36.20 ± 5.7	$F_{2,64}$ = 3.32, p<.05	Nil
Disease duration	6.41 ± 3.7	8.05 ± 4.5	12.94 ± 7.5	$F_{2, 101}$ = 12.02, p<.0001	PD-N v PD-D p < .001 PD-MCI v PD-D p < .001
GDS[c]	1.13 ± 2.3	1.33 ± 2.5	1.5 ± 2.4	$F_{2,92}$ < 1.0	
HADS[d]	4.7 ± 2.7	7.35 ± 3.1	7.5 ± .7	$F_{2,41}$ < 1.0	
ADL-IS[e]	.54 ± .5	.68 ± .4	2.04 ± .6	$F_{2,91}$ = 34.63, p <.0001	PD-N v PD-D, *p* < .001 PD-MCI v PD-D *p* < .001

Values reported as mean ± standard deviation; Eth:NZer = Ethnicity New Zealander/*Other = Chinese, Vietnamese and Mixed; NPI (n=94) Neuropsychiatric Inventory; UPDRS Unified Parkinson's Disease Rating Scale; GDS Geriatric Depression Inventory; HADS Hospital Anxiety and Depression Scale; ADL-IS Activities of Daily Living – International Scale (max=4.0); [a] n=56 PD-N, 31 PD-MCI, 7 PD-D; [b] n= 38 PD-N, 24 PD-MCI 5 PD-D; [c] n= 56 PD-N, 31 PD-MCI, 7 PD-D; [d] n= 22 PD-N, 20 PD-MCI, 2 PD-D; [e] n=56 PD-N, 31 PD-MCI, 7 PD-D.

Table 3-2. Caregiver demographic variables.

	PD-N	PD-MCI	PD-D	Analysis
n	57	31	16	
Age	65.2 ± 9.6	62.2 ± 13.3	67.9 ± 11.7	$F_{2,101}$ <1.0
Female/Male	2.4:1	2.4:1	3:1	
Years Education	12.3±2.1	12.3±2.7	11.5±1.8	$F_{2,101}$ <1.0
Eth:NZer/Other*	54/3	30/1	16/0	
Spouse/Other[b]	53/4	25/6	13/3	
Lives separately	3	7	5	
PAC[c]	26.9±8.9	25.48±9.8	24.3±9.3	$F_{2,101}$<1.0

Scores reported as mean ± standard deviation; Eth:NZer = Ethnicity New Zealander/*Other = Chinese, Vietnamese and Mixed; [b]Daughter, son, daughter-in-law, brother or friend; [c]PAC Positive Attributions of Caregiving

3.1 The Influence of Cognitive Status on Caregiver Outcome

Mean Zarit Burden scores differed significantly between caregivers for patients across the 3 cognitive status groups (F (2,101) = 9.96, p < .001) (Figure 3-1a). Caregivers for PD-MCI patients had Zarit Burden ratings that were intermediate to those caregivers for PD-N and PD-D patients. Post hoc tests (Newman-Keuls) confirmed significant differences between all 3 groups: PD-N versus PD-MCI, p < .05; PD-N versus PD-D, p < .001; and PD-MCI versus PD-D, p < .05. Analyses of effect sizes for the differences between groups identified large effect sizes between PD-N versus PD-D (Cohen's d = 1.2) and PD-MCI versus PD-D (Cohen's d = .62) and a medium effect size between PD-N versus PD-MCI (Cohen's d = .59). The proportion of carers showing significant burden scores (Zarit burden

score ≥ 21; Zarit, Reever, & Bach-Peterson, 1980) was 21% for PD-N, but rose to 58% for PD-MCI and 81% for PD-D (χ^2 = 23.73, p < .001). All PD-D patients had received full assessment that confirmed their diagnostic status. Most other PD patients received full assessment (n = 62) to validate PD-N versus PD-MCI cognitive status but some patients (n = 28) had only brief assessments. The factor *full* versus *brief* assessment was therefore used in a supplementary analysis. There was no significant interaction between the effects of PD patient cognitive status and full versus brief cognitive assessment on mean Zarit burden scores (F(2, 84) < 1.0) and no overall differences in Zarit burden scores between carers of patients with full (mean=17.66, SE = 1.5) versus brief (mean = 17.51, SE = 2.6) cognitive assessment (F(1, 84) < 1.0) . As expected, differences between PD-N (mean = 14.03, SE = 1.6) and PD-MCI (mean = 21.14, SE = 2.5) caregiver burden scores remained significant (F(1, 84) = 5.47, p < .05). Hence the total sample of PD-N and PD-MCI patients was regarded as valid.

Unified Parkinson's Disease Rating Scale scores (n = 67) available from patients within 4 months of caregiver interview did not correlate with caregiver burden (r(102) =.09). Moreover, the significant effect of patient cognitive status between PD-N and PD-MCI on caregiver burden remained after controlling for the effects of this PD motor rating (F(2,62)=8.96, p<.005). In a separate analysis (n = 94), neuropsychiatric scores were also included as a covariate to remove the possible confounding effects of PD patient neurobehavioural symptoms. The significant effect of patient cognitive status also remained when patient neuropsychiatric symptoms were added as a covariate F(2, 90) = 4.44, p < = .05. Additionally, in further analyses (n=104) caregiver depression and anxiety were also included as covariates, which if anything increased the Zarit burden differences between the three patient cognitive status groups (depression, F(2, 100) = 15.98, p = .0001; and anxiety, F(2, 100) = 12.71, p = .0001).

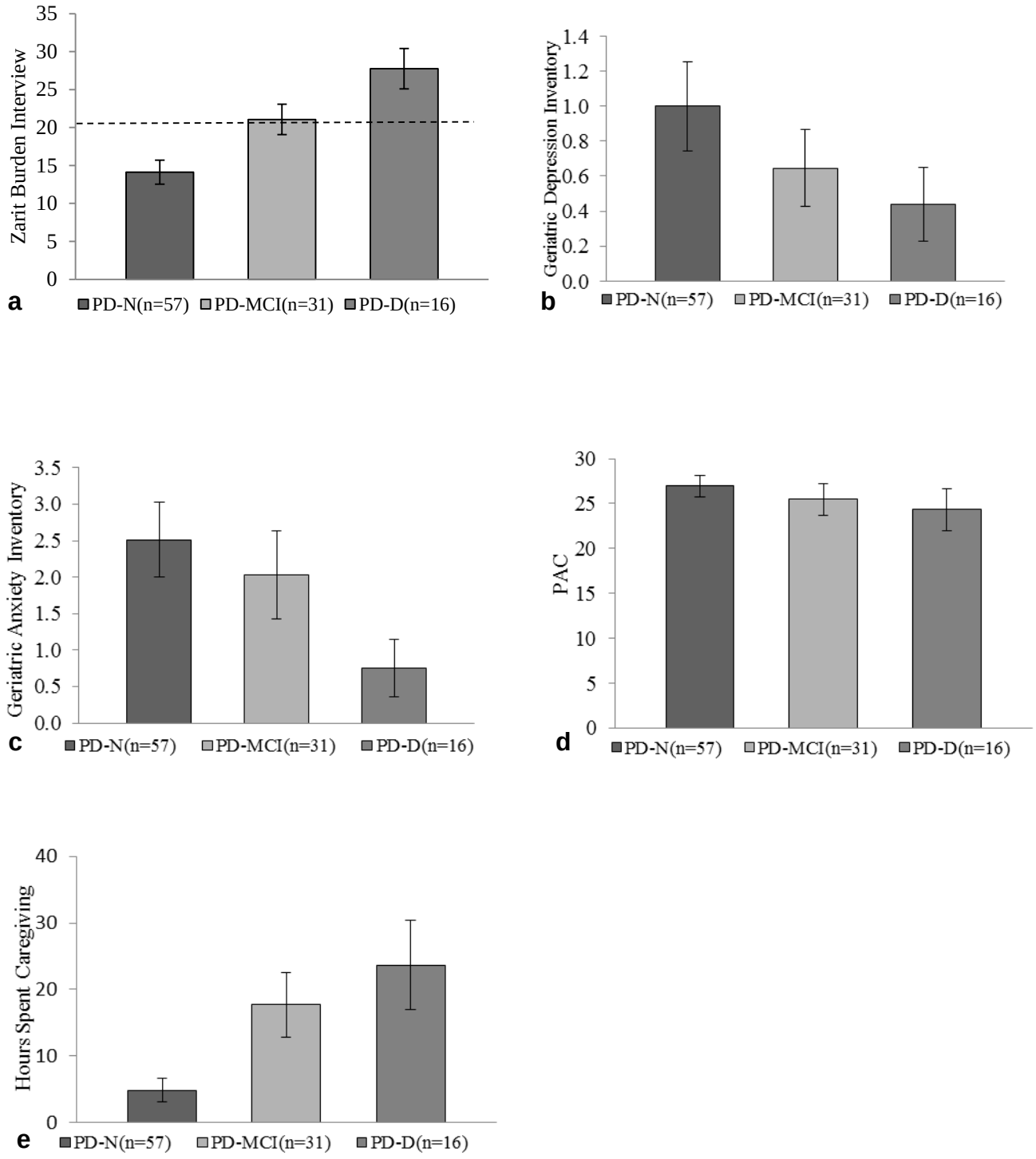


Figure 3-1

a Burden experienced by caregivers as measured with the Zarit Burden Interview as a function of cognitive status of the caregiver; b Mean depression scores of caregivers as a function of cognitive status of the PD patients; c Mean anxiety scores of caregivers as a function of cognitive status of the PD patients; d Positive Attributions towards caregiving as expressed by caregivers as a function of the PD patients; e Mean number of hours spent caregiving as a function of cognitive status of the PD patients.

3.2 Anxiety, Depression and Positive Attributions in Caregivers as a Function of PD Patient Cognitive Status

Seven per cent of caregivers and 10% of PD patients had symptoms of mild depression as measured with the Geriatric Depression Scale (GDS score > 5/15;Weintraub, Oehlberg, Katz, & Stern, 2006). Mean GDS scores did not differ significantly between caregivers for patients in the 3 cognitive status groups (F (2,101) = 2.09, p =.13) (Figure 3-1b). There was a significant but low correlation between the depression scores of the caregivers and those of the PD patients as measured with the GDS: r(93)=.22, p<.05.

Thirty-six percent of all caregivers (n=104) scored in the mild anxiety range and 8% of these scored in the possible anxiety disorder range. Mean Geriatric Anxiety Inventory scores did not differ significantly between caregivers for patients in the 3 cognitive status groups (F (2,101) = 1.61, p = .20) (Figure 3-1c). Among PD-D caregivers 25% had mild anxiety (≤ 8 and ≥2; Pachana et al., 2007) but none had a possible anxiety disorder (GAI score ≥ 9;Pachana et al., 2007). 32% PD-MCI caregivers had mild anxiety and 7% presented with a possible anxiety disorder. 42% PD-N caregivers had mild anxiety and 9% had a possible anxiety disorder. Patient anxiety scores (HADS) did not correlate significantly with GAI caregiver scores r(43) = -.07, ns.

Positive Attributions towards Caregiving scores did not differ between caregivers in the three cognitive status groups (Figure 3-1d).

3.3 Time Spent Caregiving.

The number of hours that caregivers spent per week caring for PD patients increased significantly between caregivers in the 3 cognitive status groups (F(2, 101) =7.04, p < .01) (Figure 3 1e). Post hoc tests showed a significant difference between PD-N versus PD-MCI p < .05, PD-N versus PD-D p < .01, but it was interesting that this was not the case not between PD-MCI versus PD-D p = .29. Analyses of effect sizes for the differences between groups identified medium to large effect sizes between PD-N versus PD-MCI (Cohen's d = .60) and PD-N versus PD-D (Cohen's d = .88) but only a small effect size between PD-MCI and PD-D (Cohen's d = .22).

3.4 Gender differences

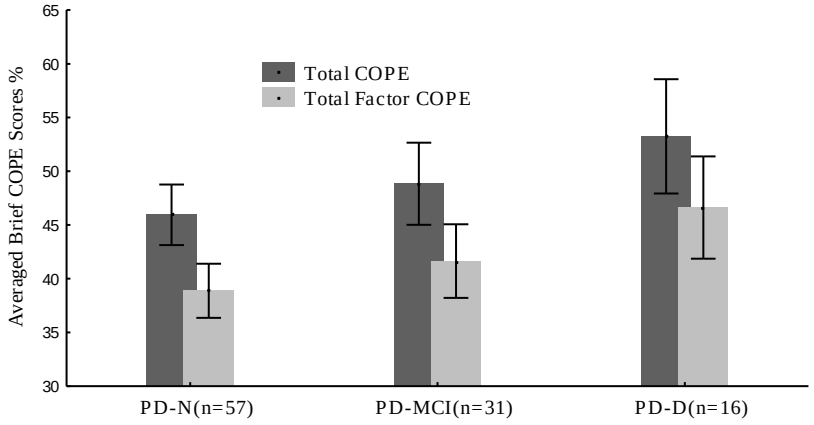
There were no significant differences in Zarit burden scores between female and male caregivers in PD-N ($t(55) = .91$, $p = .36$); PD-MCI ($t(29)=.44$, $p = .66$) and PD-D ($t=.58$, $p = .56$) (Table 3-3).

Table 3-3. Gender differences in mean Zarit burden scores.

	Zarit Burden Score		
	Female	Male	F/M
PD-N	15.07(n=40)	11.88(n=17)	2.4:1
PD-MCI	21.64(n=22)	19.67(n=9)	2.4:1
PD-D	28.67(n=12)	25(n=4)	3:1

3.5 Caregiver Coping

The total mean score of all 28 coping items also increased significantly as a function of the patients' cognitive status ($F(2, 101) = 3.09$, $p < .05$) (Figure 3-2). Post hoc tests (Newman-Keuls) showed significantly lower total scores in PD-N versus PD-D caregivers ($p<.05$) but not between PD-N versus PD-MCI caregivers ($p = .32$) or PD-MCI versus PD-D caregivers ($p = .13$). Analyses of effect sizes for the differences between groups identified a small effect size between PD-N versus PD-MCI (Cohen's $d = .22$), a medium effect size for PD-MCI versus PD-D (Cohen's $d = .55$) and a large effect size between PD-N and PD-D (Cohen's $d = .84$). Three dimensions of coping, problem-focused, emotion-focused and dysfunctional were identified from the 28 items of the Brief COPE with factor analysis, which is described in detail in Appendix D. Restricting total mean scores to the factor derived dimensions yielded similar results: Total mean factor derived scores increased significantly between caregivers of patients in the 3 cognitive status groups $F(2,101) = 4.21$, $p < .05$ and post hoc tests showed significantly lower total scores in PD-N versus PD-D patients ($p < .05$) but not between PD-N versus PD-MCI patients ($p = .29$) or PD-MCI versus PD-D patients ($p = .06$). Female caregivers employed more coping strategies in total than males ($t(104)= 2.1$, $p < .05$).



COPE Coping Orientations for Problems Experienced

Figure 3-2. Total mean scores for number of coping strategies used by caregivers as a function of cognitive status of the PD patients (n=104).

The use of coping strategies by PD caregivers was examined for each of the 3 dimension scores derived from the factor analysis of the Brief COPE instrument (Figure 3-3). The factor derived dimensions, problem-focused coping, emotion-focused coping and dysfunctional, excluded the 2 self-blame items, 2 denial items and 1 positive reframing item. As the emotion-focused dimension contained 7 items and the problem-focused and dysfunctional dimensions contained 8 items, scores were averaged and are provided in Table 3-4. There was no difference between the 3 cognitive status groups in the use of emotion-focused coping ($F(2, 101) = 1.70$, $p = .19$) or dysfunctional coping strategies ($F(2, 101) = 1.95$, $p = .15$). However there was a significant difference between the groups in the use of problem-focused coping strategies ($F(2, 101) = 4.05$, $p < .05$). Post hoc tests (Newman-Keuls) revealed that PD-N caregivers used significantly less problem-focused coping strategies than PD–D ($p < .05$); PD-MCI caregivers used less than PD-D ($p < .05$); there was no difference between PD-N versus PD-MCI ($p = .39$) in problem-focused coping. Analyses of effect sizes for the differences between groups identified a small effect size between PD-N versus PD-MCI (Cohen's $d = .23$), and medium to large effect sizes between PD-N versus PD-D (Cohen's $d = 94$) and PD-MCI and PD-D (Cohen's $d = = .67$).

Table 3-4. Subscale scores on the Brief COPE

	PD-N	PD-MCI	PD-D
Brief COPE[a]			
Problem-focused Dimension[b]	1.85±	2.01±	2.38±
Active Coping[c]	1.89±0.79	2.06±0.91	2.44±0.91
Emotional Support[c]	1.82±0.90	1.81±0.74	2.22±0.77
Instrumental Support[c]	1.57±0.65	1.82±0.76	2.25±1.10
Planning[c]	2.14±0.86	2.34±1.03	2.63±0.81
Emotion-focused Dimension[b]	1.95±	2.12±	2.21±
Positive Reframing 2[c]	1.95±0.87	2.32±2.01	1.81±0.98
Humour[c]	1.50±0.65	1.90±0.89	1.91±0.76
Acceptance[c]	2.77±0.96	3.00±1.05	3.44±0.68
Religion[c]	1.66±0.94	1.53±0.90	1.34±0.57
Dysfunctional Dimension[b]	1.31±	1.34±	1.51±
Substance Use[c]	1.07±0.31	1.03±0.12	1.16±0.30
Venting[c]	1.48±0.60	1.61±0.75	1.56±0.44
Self-Distraction[c]	1.52±0.80	1.52±0.74	2.28±1.08
Behavioural Disengagement[c]	1.13±0.38	1.21±0.40	1.03±0.13

[a] High scores on the Brief COPE subscales indicate higher use of the respective coping strategy
[b] Dimension Scores derived from factor analysis of the Brief COPE described in Appendix D

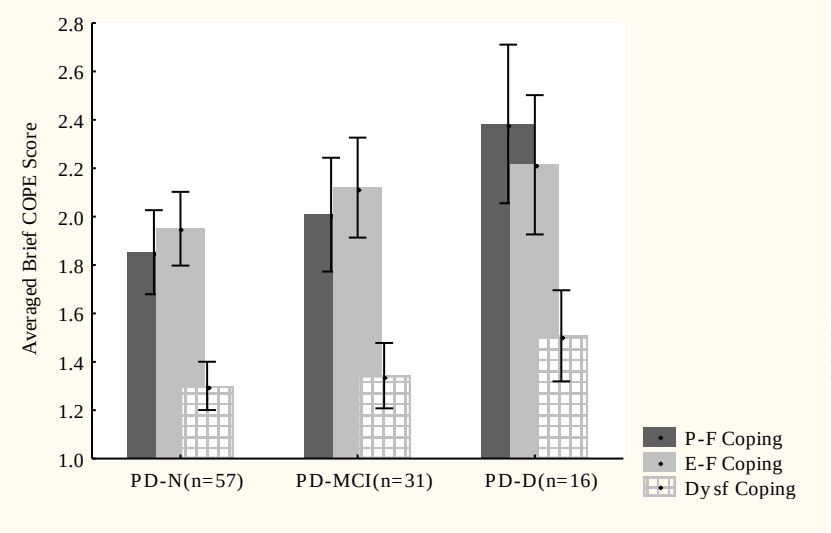


Figure 3-3. Total number of coping strategies used by caregivers as a function of cognitive status of the PD patients (n=104).

3.1 Correlations between Caregiver and PD Patient Characteristics

Four measures of PD patient cognition (z score, Montreal Cognitive Assessment, Mini-Mental State Exam and cognitive status), correlated inversely with Zarit burden, ie. more burden with lower cognitive ability (Table 3-5). All 3 types of coping strategy significantly correlated with Zarit burden but only problem-focused also correlated with PD patient cognitive status. Neuropsychiatric

symptoms, activities of daily living and disease duration also significantly correlated with both Zarit burden and cognitive status. Caregiver burden, anxiety and depression did not correlate with caregivers difficulties relating to the recent Christchurch earthquakes and aftershocks: $r(104) = -.13$, $p = .15$; $r(104) = -.15$, $p = -.14$; $r(104) = -.05$, $p = .61$ respectively.

Table 3-5 Correlations between measures of caregiver distress and clinical characteristics of the PD patients (n=104 unless otherwise stated).

	ZBI	GAI	GDS	PAC	CogStat
Patient Variables					
z score	-.20*	.14	.11	.03	.20*
MoCA score	-.21*	.17	.20*	.22*	-.59*
MMSE score	-.24*	.10	.10	.17	-.58*
Cognitive Status	-.41*	-.17	-.19	.11	1.00
Disease Duration	.47*	.21*	.27*	.09	.22*
NPI	.42*	.14	.09	.03	.38*
ADL-IS	.56*	.01	.12	-.04	.46*
PATGDS	.28*	.28*	.23*	.01	.04
UPDRS	.09	.14	.02	.13	.31*
Caregiver Variables					
Age	.01	-.13	-.06	-.20*	-.10
PMIQ	.09	-.01	.08	-.16	-.09
Hours Caring	.36*	-.03	.07	.01	.34*
P-F Coping	.56*	.09	.02	.10	-.26*
E-F Coping	.38*	.07	-.07	.25*	-.18
Dysf Coping	.68*	.30*	.19*	-.07	-.18
GAI	.18	1.00	.56*	.19	-.08
CGGDS	.29*	.56*	1.00	.01	-.17
PAC	-.01	.19	.01	1.00	-.13

Spearman correlations. * <0.05. MoCA (n=94) Montreal Cognitive Assessment; NPI (n=94) Neuropsychiatric Inventory; ADL-IS (n=94) Activities of Daily Living-Instrumental Scale; CGGDS Caregiver Geriatric Depression Inventory; PatGDS Caregiver Geriatric Depression Inventory HrsCr Hours spent caring' P-F Coping Problem-focused coping; EF Coping Emotion-focused coping; Dysf Coping Dysfunctional coping; PAC Positive Attributions towards caregiving; PMIQ Premorbid Intelligence Quotient. CogSt Cognitive Status; z score (n=67).

3.2 Mediators of Caregiver Burden

The associations between PD patient cognitive status, coping and caregiver Zarit burden were first examined to find support for the use of path analysis to examine the mediator effect of coping between PD patient cognitive status and caregiver burden (Table 3-5). Emotion focused and dysfunctional coping failed to meet criteria as there were no significant associations between cognitive status and either emotion-focused coping ($r = .17$) or dysfunctional coping ($r = .18$). However problem-focused coping was independently associated with caregiver burden and cognitive status and therefore met

criteria for path analysis (Figure 3-4). The standardized regression coefficient between cognitive status and caregiver burden (.41) decreased substantially (to .28) when controlling for problem-focused coping strategies. Both the Sobel test (www.quantpsy.org/sobel/sobel.htm) and the method suggested by Preacher and Hayes (2004) that incorporates bootstrapping to obtain a confidence interval (CI) for the mediated effect were used to assess the mediator model. A mediator is significant when the 95% CI does not include zero. The change in the model reflecting mediation was found to be significant according to both methods: Sobel test: $z = 2.56$, $p < .05$; unstandardized indirect effect from bootstrapping procedure: $b = 2.48$, $SE = .99$, CI = 0.49, 4.38. Unfortunately, we cannot rely on the directionality of this model because the inverse model with Zarit burden, instead, mediating a link between cognitive status and problem-focused coping was also significant: Sobel test: $z = 3.76$, $p<.01$; unstandardized indirect effect from bootstrapping procedure: $b = 3.56$, $SE = .06$, CI = 0.10, 0.34.

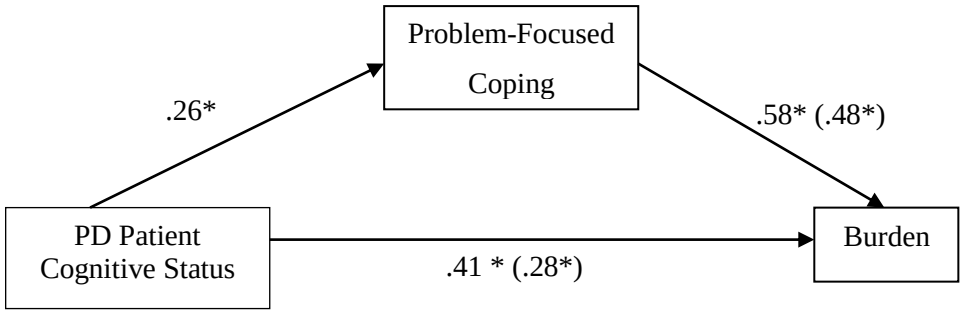


Figure 3-4. Standardized regression coefficients for the relationship between PD patient cognitive status and caregiver burden as mediated by use of coping strategies (n=104). The standardized regression coefficient between cognitive status and burden controlling for coping strategies is in parentheses *p<.05.

Patient neuropsychiatric symptoms, disease duration and activities of daily living also all met the criteria for mediation analysis: Each was independently associated with both cognitive status and caregiver burden. However by definition, activities of daily living are included in cognitive status classification and disease duration is suggestive of worsening cognition, therefore only neuropsychiatric symptoms were submitted to path analysis (Figure 3-5). The standardized regression coefficient between cognitive status (.39) and caregiver burden decreased (.26) when controlling for patient neuropsychiatric symptoms. The change in the model reflecting mediation was found to be significant: Sobel test: $z = 2.96$, $p < .01$; unstandardized indirect effect from bootstrapping procedure:

b = 2.44, *SE* = .96, CI = 0.41, 5.38. The inverse model (Zarit burden mediating the association between cognitive status and NPI) was not examined as it is not theoretically possible.

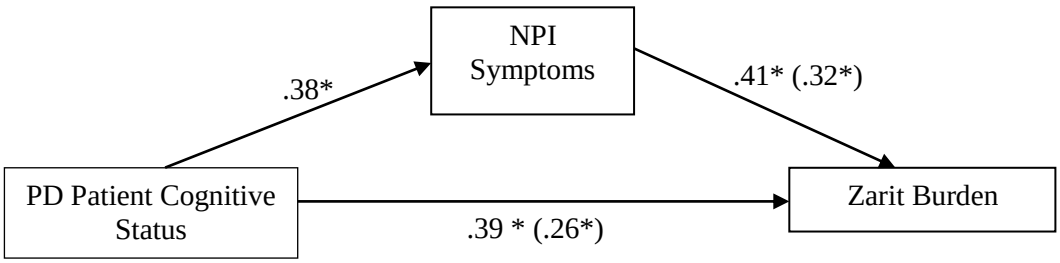
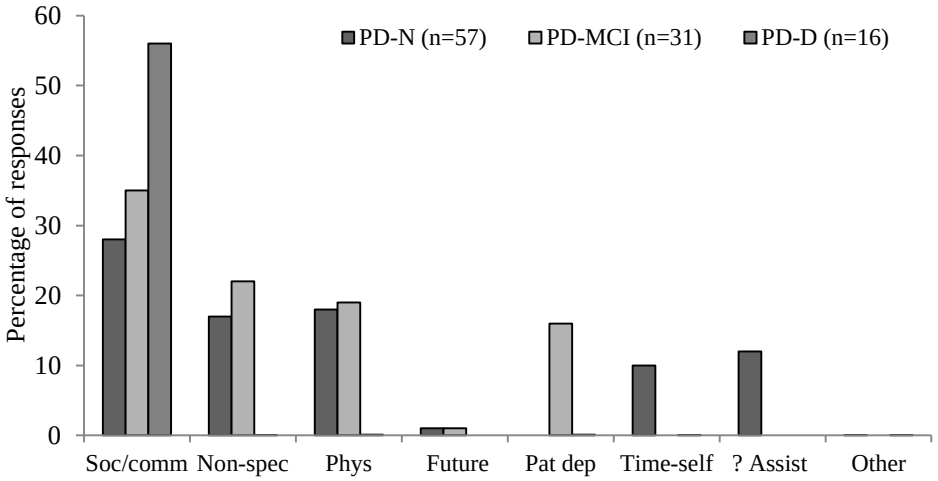


Figure 3-5. Standardized regression coefficients for the relationship between PD patient cognitive status and caregiver burden as mediated by PD patient neuropsychiatric symptoms (n=94). The standardized regression coefficient between cognitive status and burden controlling neuropsychiatric symptoms is in parentheses *p<.05.

The "Hardest Thing"

The caregiver responses to the open-ended question, "What is the hardest thing about providing support to someone with Parkinson's disease?" is provided in Figure 3-6. The majority of caregivers reported that it was the impact/drawback of reduced personal or social communication that they found most challenging. eg. "I have lost my best friend." Examples of 'Non-specific' responses included "Nothing in particular" and "He's so grumpy and irritable now." Example of 'Other' included "It took two years before doctors could provide a diagnosis". Fifty six percent of PD-D caregivers felt that social communication was the "hardest thing" compared with 35% PD-MCI and 28% PD-N.



Soc/comm Personal and social communication; Non-spec Nothing or not specific to PD' Phys Physical symptoms of PD; Pat dep Patient dependence on caregiver; Time-self Time for self; ? Assist Being unsure whether to help the PD patient or not; Other Specific individual concerns.

Figure 3-6. The percentage of caregiver responses to the question "What is the hardest thing about providing support/care to someone with Parkinson's disease?" as a function of cognitive status of the PD patients (n=104).

4 DISCUSSION

The current study sought to investigate the impact of PD patient cognition on caregiver outcome including caregiver burden, depression and anxiety. Additionally, the potential mediating effects of caregiver coping strategies and positive attributions towards caregiving between PD patient cognitive status and caregiver burden were examined. A qualitative question "What is the hardest thing about providing support/care for someone with Parkinson's disease" was added to provide an insight to the carer's global perspective.

4.1 Summary of Findings

Patients in the current study were classified as showing PD-N, PD-MCI or PD-D. The caregiver mean Zarit burden scores increased significantly between caregivers for patients between each of these three cognitive status groups. This investigation reports for the first time increased burden among carers of PD-MCI patients compared with those of PD-N. The findings were in contrast to the only other study to investigate caregiver burden for patients classified as PD-MCI (Leroi, McDonald, Pantula, & Harbishettar, 2012). Leroi and colleagues (2012) reported that although the mean burden score for PD-MCI caregivers (23.61) was above the ≥ 21 threshold set by Zarit (Zarit, Reever, & Bach-Peterson, 1980) this was similar to the mean burden score for PD-N caregivers (20.41). Only caregivers of PD-D patients showed relatively increased burden (35.48).

The total mean coping scores also increased with worsening cognition. PD-MCI caregivers' total scores were intermediate to PD-N and PD-D caregivers with a large difference in values between PD-N versus PD-D caregivers. Problem-focused coping, however, was the only strategy to differ between caregivers for patients in the three cognitive status groups with a similar pattern to that evident for total coping strategies. All three coping strategies were associated with caregiver Zarit burden, but only problem-focused coping strategies were associated with cognitive status. The relationship between PD patient cognitive status and caregiver burden may in part be mediated by caregiver problem-focused coping, as well as patient neuropsychiatric symptoms.

Caregiver symptoms of depression and anxiety were not associated with cognitive status. The rates of depression symptoms among the caregivers were less than those reported in other PD

caregiving studies (Caap-Ahlgren & Dehlin, 2002; Martinez-Martin et al., 2008; Meara, Mitchelmore, & Hobson, 1999), while rates of anxiety symptoms were greater in comparison with other similar investigations (Martinez-Martin et al., 2008).

Caregivers spent more time caring with worsening cognition and PD-MCI caregivers spent time that was close to PD-D caregivers. These between group differences were large between PD-N versus PD-MCI and between PD-N and PD-D. The additional qualitative question: "What is the hardest thing about providing support for someone with Parkinson's disease?" showed that social communication was the most common concern among carers, which was more frequent in the PD-D carers.

Sample Characteristics Compared with Other PD Caregiving Studies

The composition of the PD Patients and caregivers was comparable to recently published PD caregiving patient samples in terms of PD diagnostic methods, range of cognitive impairment, gender, age and education (Table 1-1 and Table 1-2). Among previously published PD caregiving studies there was some heterogeneity in use of the term 'caregiver'. However the current sample compared well with the majority of publications in the inclusion of spouse, family and friend caregivers as well as the amount of time spent caregiving.

There was an under-representation of ethnic minorities in the current study. In the case of Māori and Pacific Islanders this may reflect reluctance to access healthcare including involvement in research (McPherson, Harwood, & McNaughton, 2003). Nonetheless, estimates by researcher Toni Pitcher (NZBRI) using recent Pharmac database prescription data, suggest the prevalence of PD in Māori is half that for non- Māori.

The current sample was considered to be representative of other PD caregiving populations.

4.2 Cognitive Status

Caregiver Zarit Burden

The main aim of the study was to investigate the influence of PD patient cognitive status on caregivers. Specifically, the cognitive status of the patients was assessed using recently published guidelines by the Movement Disorders Task Force thus describing the patients as PD-N, PD-MCI or

PD-D (Emre et al., 2007; Litvan et al., 2012). The primary outcome variable for caregivers was Zarit burden and mean burden scores increased significantly between caregivers in the three cognitive status groups: PD-D caregivers had significantly higher Zarit burden scores compared to both PD-N and PD-MCI caregivers but carers of PD-MCI patients also showed increased burden scores relative to those of PD-N patients. No gender caregiver Zarit burden score differences were found and the significant effects of PD patient cognitive status remained after controlling for both PD patient motor problems and neuropsychiatric symptoms. The results highlight the progressive nature of caregiver burden in the context of worsening PD patient cognition and provide support for the description of PD-MCI as a clinical identity that has a significant impact.

Previous research has reported conflicting results regarding the influence of cognitive status on caregiver burden, but this may be in part due to restricted outcome measures. For example when the Zarit burden instrument was employed, all three studies reported that PD patient cognition was associated with burden (Cifu et al., 2006; Leroi, McDonald, Pantula, & Harbishettar, 2012; Martinez-Martin et al., 2008), a finding supported in the current research. However in studies using depression, distress or health measures as outcome instruments, no associations were found (Fernandez, Tabamo, David, & Friedman, 2001; Lee, McKeith, Mosimann, Ghosh-Nodyal, & Thomas, 2012; Meara, Mitchelmore, & Hobson, 1999; Miller, Berrios, & Politynska, 1996).

The increase in Zarit burden scores between PD-N, PD-MCI and PD-D caregivers, was in contrast to the only other study to use MDS criteria to describe cognitive status in PD caregiving (Leroi, McDonald, Pantula, & Harbishettar, 2012). These authors reported differences between PD-N and PD-MCI versus PD-D but none between PD-N versus PD-MCI. PD-MCI caregivers in the current study experienced similar burden (mean Zarit burden = 20.65) to those in the Leroi study (mean Zarit burden= 23.61) but the PD-N and PD-D caregivers in the study by Leroi and colleagues were more burdened (mean Zarit burden=20.41 and 35.48 respectively), compared with those in the current study (mean Zarit burden=13.48 and 26.84 respectively). Perhaps the more comprehensive neuropsychological battery (20 tests) used in the current study provided greater diagnostic accuracy than the eight tests employed in the study by Leroi and colleagues (2012). Another explanation for the

contrary findings is different sample characteristics: PD-N mean neuropsychiatric inventory scores in the current study (3.4) were much lower than the mean neuropsychiatric inventory scores in the Leroi study (9.5) which in conjunction with cognitive deficits may have lead to greater caregiver burden amongst their PD-N caregivers.

Forty one percent of caregivers in the current study scored ≥21 on the Zarit burden Interview indicating mild to severe burden (Zarit, Reever, & Bach-Peterson, 1980). While there was no information regarding the proportion of caregivers with Zarit burden scores ≥21 among other PD caregiving studies, reports from other caregiving studies have provided rates of 30% among muscular dystrophy caregivers (Boyer, Drame, Morrone, & Novella, 2006) and approximately 55% among caregivers of the elderly (Hebert, Bravo, & M, 2000). PD-MCI caregivers in the current study demonstrated higher rates of Zarit burden (58%) than the 30%-31.4% rates reported in Alzheimer's studies of caregivers of patients with mild cognitive impairment (Bruce, McQuiggan, Williams, Westervelt, & Tremont, 2008; Hayashi et al., 2013; Springate & Tremont, 2012). The additional motor and neuropsychiatric symptoms of

The current investigation used the Mini-Mental State Exam (MMSE) as part of the neuropsychological assessment to establish global mental status. The significant negative correlation found between all PD patients' MMSE scores and negative caregiver outcome replicated the findings of Aarsland (1999), Cifu (2006) and Thommessen (2002) but were in contrast to those of D'Amelio (2009) and Fernandez (2001). Unlike the current, to establish PD-D two investigations used the Dementia Rating Scale (Table 1-1) to identify PD-D. The significant association between PD-D and caregiver burden was not replicated in these studies. Cifu and colleagues (2006) reported no association and in the other study, dementia status was associated with but not predictive of caregiver stress (Aarsland, Larsen, Karlsen, Lim, & Tandberg, 1999). The significant negative correlations between Montreal Cognitive Assessment (MoCA) scores (n=104), MMSE scores (n=67) and z scores (n=67) with Zarit burden in the current investigation further substantiated the influence of PD patient cognition on caregiver outcome.

Caregiver Depression and Anxiety

There were no significant differences between caregiver depression scores across the three PD patient cognitive status groups. Contrary to the hypothesis that caregivers would respond to worsening PD patient cognition with reports of more depression symptoms, caregivers demonstrated fewer depression symptoms with worsening cognition (Figure 3-1b). This finding may reflect an acceptance over time to the diagnosis of PD and indicate positive adjustment in the caregiving role. Another explanation, in light of the negligible relationship between PD patient cognition and caregiver depression described earlier, is that Zarit burden identifies a unique contribution of distress in caregivers quite independent of depression. Another point of interest was the incidence of caregiver depression symptoms (7%), which were much lower than rates reported in other PD caregiving samples (34-64%) (Caap-Ahlgren & Dehlin, 2002; Meara, Mitchelmore, & Hobson, 1999) but similar to those reported in the general NZ population (6%; Ministry of Health, 2006). In two Alzheimer studies caregivers of patients with mild cognitive impairment rates of 12.5% (Blieszner & Roberto, 2010) and 23% (Seeher, Low, Reppermund, & Brodaty, 2012) were provided. Again the low incidence of depression in the current sample may reflect acceptance and adjustment in the caregivers or may indicate poor applicability of the Geriatric Depression Scale in this sample of caregivers whose ages ranged from 23 to 83 years: The Geriatric Depression Scale was designed as an instrument for older populations.

Caregiver anxiety symptoms also did not differ between caregivers in the three PD patient cognitive status groups and caregivers reported fewer anxiety symptoms with worsening cognition (Figure 3-1c). Again this finding may reflect acceptance and adjustment to the role of PD caregiving or highlight a unique contribution of Zarit burden quite independent of anxiety. Additionally, the Geriatric Anxiety Inventory was designed as an instrument for use in older populations and may therefore be unsuitable for use in the current sample with its wide range of ages. Rates of anxiety symptoms among caregivers in the current study (36%) were greater than that reported in the only other PD study investigating caregiver anxiety (21.7%) (Martinez-Martin et al., 2008) and greater than that reported in the general population (14.8%; Ministry of Health, 2006). Additionally, caregivers in

the current study expressed more symptoms of anxiety (36%) than Alzheimer's caregivers (23.5%-25%) (Cooper, Katona, Orrell, & Livingston, 2008; Mahoney, Regan, Katona, & Livingston, 2005). The additional neuropsychiatric and motor symptoms of PD appear to compound caregiver anxiety. Perhaps PD with its complex presentation creates increased anxiety among caregivers because of the need to maintain heightened vigilance related to potential threats in the environment for the PD patient.

The incidence of depression symptoms (7%) among caregivers in the current study was similar to that reported by their respective PD patients (10%). Likewise, the incidence of anxiety symptoms among caregivers (36%) was also similar to that reported by the PD patients (35%) although there were a limited number of PD patient anxiety scores available (n=44). The low incidence of depression in caregivers in the current study may be the result of a low incidence of depression in the current PD patients' which is also much lower than rates reported among their respective PD patients. The effect of a care recipient's distress on caregivers has become a recent area of interest (Goodman & Shippy, 2010): Early studies highlight an affect similarity or emotional contagion which may explain the almost identical incidence of depression and anxiety symptoms in the current PD patients and their caregivers.

Caregiver Coping

Caregivers responded to increasing burden with use of more total coping strategies but these differences were only large between PD-N versus PD-D patients; effect sizes were medium between PD-N versus PD-MCI patients and PD-MCI versus PD-D patients (Figure 3-2). The brief COPE instrument was subject to factor analysis and 3 dimension scores were derived, problem-focused, emotion-focused and dysfunctional coping (see Appendix D for a description of the factor analysis methods and results).

There were significant positive correlations between all three types of coping and caregiver burden (Table 3-5). Hence the hypotheses that problem-focused and dysfunctional coping are associated with caregiver Zarit burden was supported and is consistent with the results from the study

of Alzheimer's caregivers by Cooper and colleagues (2008). The only PD caregiving study to investigate coping (Sanders-Dewey, Mullins, & Chaney, 2001) and two further Alzheimer's caregiving studies reported similar findings although a different instrument, the Ways of Coping Checklist was used and comparison is limited (Chou, LaMontagne, & Hepworth, 1999; Montoro-Rodriguez & Gallagher-Thompson, 2009; Sanders-Dewey, Mullins, & Chaney, 2001). The findings are consistent with the theory by Lazarus which holds that attempts to change an unchangeable situation, such as the progressive debilitating disease of PD, will result in distress.

With regard to emotion-focused coping the hypothesis that emotion-focused coping would protect caregivers from Zarit burden was not supported. While Sanders-Dewey and colleagues (2001) reported a positive association between emotion-focused coping and caregiver distress, in the Ways of Coping Checklist emotion-focused coping contains some items that are more similar to dysfunctional coping and so comparison is precluded. However the results of the current study are consistent with those from Cooper and colleagues (2008) who reported that emotional coping was adaptive. The finding that there were significant correlations between all three types of coping and caregiver burden in the current sample, may be of increased anxiousness: Caregivers therefore had an increased tendency to take proactive actions by using all three types of coping in an attempt to reduce their stress.

Problem-focused coping was the only coping strategy to differ significantly between caregivers in the 3 patient cognitive status groups: PD-N caregivers used significantly less problem-focused coping strategies than PD–D and PD-MCI caregivers used significantly less problem-focused coping strategies than PD-D; there was no significant difference between PD-N and PD-MCI caregivers in problem-focused coping. The significant effect of patient cognitive status on Zarit burden remained after controlling for the effects of problem-focused, emotion-focused and dysfunctional coping which demonstrated that coping strategies were ineffective in reducing Zarit burden.

Patient Neuropsychiatric Symptoms

Consistent with other studies investigating the impact of PD patient neuropsychiatric symptoms on caregivers (Aarsland et al., 2007; Leiknes, Tysnes, Aarsland, & Larsen, 2010), the current study found a significant association between Neuropsychiatric Inventory (NPI) ratings and caregiver Zarit burden. There was also a significant association between NPI ratings and cognitive status. This unexpected finding enabled further investigation with path analysis to investigate a possible mediating effect of neuropsychiatric symptoms between PD patient cognitive status and caregiver burden. A relationship between these variables was suggested by Aarsland and colleagues (2007). The authors identified an agitation cluster within the Neuropsychiatric Inventory and reported that patients in this cluster achieved significantly lower scores on the Mini-Mental State Exam than those in the other clusters.

Time Spent Caregiving

An unexpected finding in the current study was a significant difference in the number of hours spent caregiving between the three patient cognitive status groups. By definition, PD-MCI patients are not impaired in their ability to undertake activities of daily living but PD-MCI caregivers spent significantly more time engaged in providing care than PD-N caregivers. This implies that even in the early stages of the disease impaired cognition alone places additional demands on caregivers and provides support for the description of PD-MCI as a clinical identity that has a significant impact.

4.3 Mediators of PD Patient Cognitive Status and Caregiving Zarit Burden

Problem-focused coping was the only coping dimension that met the criteria for path analysis. Problem-focused coping mediated the relationship between PD patient cognitive status and caregiver Zarit burden. However, the inverse model with caregiver Zarit burden mediating the link between cognitive status and problem-focused coping was also significant therefore we cannot be confident about the directionality of this relationship to draw conclusions from the findings. Uncertainty over the directionality of this relationship was also reported in a previous investigation of caregivers of the elderly (Del-Pino-Casado, Frias-Osuna, Palomino-Moral, & Pancorbo-Hidalgo, 2011). In the current study we were unable to confirm whether problem-focused coping led to caregiver burden or whether

caregiver Zarit burden led to use of problem-focused coping. Perhaps in the early stages of PD caregivers employ problem-focused strategies which prove ineffective in reducing burden, and then overtime their increased burden leads to further problem-focused coping. Future studies which are longitudinal in design could better assess the temporal course of these events.

Neuropsychiatric symptoms also mediated the relationship between PD patient cognitive status and caregiver Zarit burden. This finding suggested that caregivers of PD patients who reported more neuropsychiatric symptoms with lower cognitive ability were more likely to experience burden, and is consistent with the evidence from Aarsland and colleagues (Aarsland et al., 2007). Over and above the influence of neuropsychiatric symptoms however, PD cognitive status has the foremost influence on Zarit burden scores. Again longitudinal studies could better assess the influence of these individual factors over time.

The hypothesis that Positive Attributions of Caregiving would mediate the relationship between PD patient cognitive status and caregiver Zarit burden was not upheld. Indeed there was no association between the Positive Attributions towards Caregiving Instrument and any of the caregiving outcome variables, but this may reflect its unsuitability with PD caregivers. The measure has previously been validated with Alzheimer's dementia caregivers and may not have applicability in a sample of PD caregivers because of the heterogeneous symptoms associated with this disease. While some caregivers expressed strong positive feeling towards their role, others reported that the measure "did not capture their experience at all". Since the positive feelings among some caregivers were undeniable, it could be that improved future instruments may identify the important construct of positivity that the Positive Attributions of Caregiving failed to recognize.

4.4 "The Hardest Thing"

The majority of caregivers of PD patients in the three cognitive status groups reported that the "hardest thing about providing care/support to someone with Parkinson's disease" was the impact of reduced personal and social communication. Although this problem was most frequent in PD-D carer's and did not seem to be influenced by PD-MCI status. Motor symptoms of PD were only the third most reported item. Patients' abilities to communicate and relate to others have also been cited as causes of

caregiver burden and distress in previous general caregiving studies (Savundranayagam, Hummert, & Montgomery, 2005; Vitaliano, Russo, Young, Teri, & Maiuro, 1991).

4.5 Limitations

The caregivers and patients in the current study were already involved in other studies at the NZBRI including progression studies. This includes on-going neuropsychological assessment and scanning over several visits. The substantial time commitment by both patient and caregiver suggest that the sample in the current study were quite motivated and physically able individuals, which may influence measures such as anxiety and depression in these samples.

Time constraints in the current investigation lead to fewer data being available for PD-D patients. Specifically, fewer than half the PD-D patients had current Unified Parkinson's Disease Rating Scale scores which limited the description of the association between motor symptoms and caregiver burden.

The current study was cross-sectional in design and therefore was limited it is ability to determine causality. However, the study's strengths lie in the well-characterised PD patients who had undertaken comprehensive neuropsychological assessment to ensure robust cognitive status classification. Also the addition of the complementary qualitative question "What is the hardest thing about supporting/caring for someone with Parkinson's disease?" provided further evidence of the significant impact of PD patients' cognitive status on caregiver burden.

4.6 Future Directions

Longitudinal studies of PD patients would provide valuable information regarding those at greatest risk of progressing to PD-D. In light of the findings of the current study, which demonstrate that patient symptomology is associated with caregiver outcome, longitudinal investigations of PD caregivers may also add weight to this evidence as well as provide important insight into the changes overtime to the caregiving role in PD.

Similarly, investigations of the neural correlates of cognitive impairment have provided excellent information regarding which patients are likely to convert from PD-MCI to PD-D. Studies of

the neural correlates of Zarit burden could support evidence from this research and provide information for caregivers to enable physical and emotional provision for disease progression. Specifically, patient quality of life has been shown to be associated with executive function and visuo-spatial impairments and these too may be associated with caregiver burden.

4.7 Concluding Remarks

This research investigated the impact of PD patient cognitive status on caregiver burden. Previous studies have established that PD-D is associated with caregiver distress but the current investigation also found elevated levels of Zarit burden among PD-MCI caregivers, highlighting for the first time, the presence of Zarit burden prior to the onset of dementia. The unique experience of PD-MCI caregivers was further highlighted by the finding that PD-MCI caregivers spent significantly more time caregiving than PD-N caregivers but less than PD-D.

In agreement with previous reports (Aarsland et al., 2007; Leiknes, Tysnes, Aarsland, & Larsen, 2010), the current study found that cognitive symptoms and neuropsychiatric symptoms are contributors of negative outcomes for caregivers. There was however no associations between PD patient motor problems and caregiver Zarit burden, depression or anxiety.

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6 APPENDICES

Appendix A: Ethical Consent Form and Information Sheet

Appendix B: PD Patient Cognitive Assessment Instruments

Appendix C: Caregiver Questionnaires

Appendix D: Factor Analysis of the Brief COPE

6.1 Appendix A

66 Stewart Street, Christchurch, New Zealand

Telephone +64 3 378 6097 Fax +64 3 378 6080

CONSENT FORM

Supporting someone with Parkinson's disease"

I have read and understood the information sheet dated 1st November 2011for volunteers taking part in the study designed to gather data about supporting a person with Parkinson's disease in people in Canterbury. I have had time to consider whether to take part. I have had the opportunity to discuss this study, and I am satisfied with the answers I have been given. I have had the opportunity to use whanau (family) support or a friend to help me ask questions and understand the study. I further understand that taking part in this study is completely voluntary (my choice) and that I may withdraw from participation in this study at any time, and this will in no way affect my future health care. I understand that participation in this study is confidential and that no material which could identify me will be used in any reports of this study. I know who to contact if I have any questions or problems about the study.

I consent to my GP being informed of my participation in this study…….……YES/NO

I wish to receive a copy of the results……..…YES/NO

Name of GP……..

I consent to the information gathered about me being used for future research into studies related to Parkinson's disease (subject to ethical approval being given by a New Zealand Accredited ethics committee)……...…..…….……....YES/NO

I wish to be part of the Van der Veer Institute's volunteer database……..…….YES/NO

I consent to the use of my data for future related studies, which have been given ethical approval from a Health & Disability Ethics Committee……YES/NO

I _____*(full name)* hereby consent to take part in this study, and understand that by agreeing to be part of a volunteer database that I could be contacted again for another research study. I also understand that if I am contacted again, that I do not have to participate in that study.

Signature of Participant _____

Signature of witness _____

Project explained by _____

The following is the 2001 census form question about ethnicity. This data is collected for study demographics only

Researchers:
Ann Jones, Associate Professor John Dalrymple-Alford, Roeline Kuijer, Leslie Livingston, Professor Tim Anderson

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New Zealand Brain Research Institute

Incorporating the Van der Veer Clinics

Invitation to join the study

"Supporting someone with Parkinson's disease"

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  New Zealand Brain Research Institute

You are invited to participate in a study that will look at supporting someone with Parkinson's disease. This study will be undertaken to fulfill the requirements for the degree of Master of Arts at the University of Canterbury. You would respond to five brief questionnaires, which will take approximately 60 minutes. By taking part in the study you will help us detect the factors that influence outcomes for support people in the context of Parkinson's disease. We hope that the information we gather may help clinicians improve the quality of life for both support people and those with Parkinson's disease. You do not have to take part in the research if you prefer not to. You may withdraw at any time. With your permission, data from this study may be used in future related studies, which have been given ethical approval from a Health & Disability Ethics Committee.

1. Aim of the study

To investigate your experience as a support person for someone with Parkinson's disease.

2. Participants

People who are family members or friends of someone with Parkinson's disease are welcome to participate: They may or may not be living with the person, but need to be directly involved with the person. One hundred people who support a person with Parkinson's disease will take part in the study.

3. Your involvement

Your involvement is voluntary and you can withdraw from the study at any time without giving a reason. There will be no disadvantage to you. Your name and personal details are strictly confidential and will not be mentioned in the final report. If you decide to participate you will be asked to sign a consent form to confirm your willingness to take part in the study.

4. Interview location

The interview will be carried out either at the Van der Veer Institute or in your home. You will be reimbursed with petrol vouchers should you choose to be interviewed at the Van der Veer Institute. A family member (whanau) or support person is welcome to be present during the interview.

5. Interview Content

There will be one meeting to collect information for the study. We will ask you questions about your role in providing support to your family member or friend with Parkinson's disease. Any participants who find that some questions raise negative emotions or memories may be directed to the appropriate services: The Multiple Sclerosis and Parkinson's Society of Canterbury, GP and/or Caring for Carers. Brochures with relevant telephone numbers will be available if requested. If clinically significant information is identified during the interview, consent will be sought to inform the participants G.P.

6. Study Information Storage.

Every participant and the person with Parkinson's disease for whom support/care is provided, will be identified with a study number (no names are used). All information will be kept at the Van der Veer Institute. Only the study researchers have access to the information. Documents will be stored in a locked filing cabinet at the Van der Veer Institute. Data will be stored on the researcher's password protected computer. At the end of the study the data will be kept securely for 10 years after which time it will be destroyed.

7. Risks of the study.

There are no risks to you as a participant. The benefit of the study is that your experiences and opinion of coping with someone with Parkinson's disease may be beneficial to others in the same situation.

8. Concerns during the study

If you have any queries or concerns regarding your rights as a participant in this study you can contact the Health and Disability Advocate : 0800377766 or (03)3777501.

9. Results

It is expected that the final written report will be completed by the end of 2012. If you wish, a summary of the findings will be posted to you.

10. Ethics

This study has been given ethical approval by the Upper South A Regional Ethics Committee.
Thank-you for considering to take part in this study.

Principal researcher: Annie Jones e-mail: anniejones@xtra.co.nz
phone: 3786346 ext86346 or 0276542299

6.2 Appendix B

Significant Other/Caregiver Measures: For carers of PD Patients with Brief Cognitive Assessment

The Activities of Daily living – International Scale

The Activities of Daily living – International scale (ADL-IS; (Reisburg et al., 2001) consists of 40 questions such as "Does the [patient/subject] have difficulty putting household items in the right places?" to which the informant is asked to respond using a Likert scale of 0 = 'never has difficulty' to 3 = 'always has difficulty'. A response of 4 = 'activity no longer performed (ie. has given up initiating the activity)'; 8 = 'activity was never performed' and 9 = 'unknown'.

The Neuropsychiatric Inventory

The Neuropsychiatric Inventory (NPI;(Cummings et al., 1994) is structured interview of the significant other/caregiver used to identify possible behavioural symptoms associated with Parkinson's disease. Items assessed are: delusions, hallucinations, agitation/aggression, depression, anxiety, elation/euphoria, apathy/indifference, disinhibition, irritability/liability, aberrant motor behaviour, night-time behaviour and appetite/eating change. For each question, the informant is asked to rate the frequency (1 = 'occasionally, less than once per week,' 4 = 'very frequently – essentially continuously present'), severity (1 = 'mild, depression is distressing but usually responds to redirection or reassurance,' 3 =' marked – depression is very distressing and a major source of suffering for the patient') and distress of the patients behaviour (0 = 'not at all' to 5 = 'very severely or extremely').

Parkinson's disease Patient Measures: For PD patients who had Brief Cognitive Assessment.

Verbal Fluency (letter)

The Verbal Fluency test (Delis, Kaplan, & Kramer, 2001) is sensitive to the executive impairments seen in patients with PD. Participants are instructed to say as many words as they can that begin with a certain letter of the alphabet (F, A, or S), but not names, numbers, or places, or the same word with a

different ending. Scores are obtained from the number of correct words produced from verbal responses within 1 minute.

Action Fluency

The Action Fluency task is also a measure of executive function. Patients are instructed to say as many action words they can. The words may start with any letter and should describe things that people do (action words). Scores are taken from verbal responses and the number of correct action words produced within 1 minute.

Months Reversed

The months reversed task assesses elective attention and mental control. Participants are asked to state the months of the year backwards, beginning at December. Scoring cut-off is the omission of 2 or more months or failure to complete the test within 90 seconds (Dubois et al., 2007).

The Mini Mental State Examination

The Mini Mental Status Examination (MMSE) is a screening test designed to assess general cognitive status (Molloy & Standish, 1997). The MMSE consists of 30 questions with one point for each correct answer. The areas of cognitive functioning assessed are: orientation, registration, attention, working memory, recall, language, and construction.

The Montreal Cognitive Assessment

The Montreal Cognitive Assessment (MoCA) (Nasreddine et al., 2005) is a measure of general cognitive status. The MoCA consists of 8 components designed to measure general skills of attention and concentration, executive functions, memory, language, visuo-constructional skills, conceptual thinking, calculation, and orientation. The MoCA is scored out of 30 and is more sensitive to mild cognitive impairment than the MMSE in PD (Mamikonyan et al., 2009) (Dalrymple-Alford et al., 2010)

Parkinson's disease Patient Measures: For PD patients who had Full Cognitive Assessment

The patients were classified as either showing normal cognition (PD-N), with mild cognitive impairment (PD-MCI) or with dementia (PD-D) on the basis of neuropsychological testing (Dalrymple-Alford et al., 2011). Dementia classification was based on the Movement Disorders Society Task Force criteria (Emre et al., 2007). Mild cognitive impairment cases were defined as having generally intact functional activities of daily living but scores 1.5SDs or more below normative data on at least two measures within at least one of four cognitive domains: *executive function:* letter fluency; action fluency; category fluency; category switching;(Stroop, 1935) Stroop (Delis, Kaplan, & Kramer, 2001) Trails B (Reitan, 1958); *attention, working memory and processing speed:* digits forward and backwards, digit ordering (Kaplan, Fein, Morris, & Delis, 1991); map search (Robertson, Ward, Ridgeway, & Nimmo-Smith, 1996); Stroop-colour-naming and Stroop-word-reading; (Delis, Kaplan, & Kramer, 2001) Trails A (Reitan, 1958); *learning and memory:* California Verbal Learning Test-free recall (Elwood, 1995); California Verbal Learning Test Short Delay; Rey Complex Figure recall (Osterrieth, 1944); and *visuoperceptual and visuospatial skills* Rey Complex Figure copy (Osterrieth, 1944), Judgement Orientation (Benton, Varney, & Hamsher, 1978); fragmented letters (Warrington & James, 1991); PD-N patients do not meet the criteria for MCI. Global cognitive status was measured with the Mini Mental State Examination (Molloy & Standish, 1997) and the Montreal Cognitive Assessment (MoCA; (Nasreddine et al., 2005)). The Geriatric Depression Scale (GDS-15; (Weintraub, Oehlberg, Katz, & Stern, 2006) was also used to assess the PD patients.

6.3 Appendix C

C-1 The Zarit Burden Interview

Please circle the response the best describes how you feel. Never	Rarely	Sometimes	Quite Frequently	Nearly Always	**Score**
1. Do you feel that your relative asks for more help than he/she needs?	0	1	2	3	4
2. Do you feel that because of the time you spend with your relative that you don't have enough time for yourself?	0	1	2	3	4
3. Do you feel stressed between caring for your relative and trying to meet other responsibilities for your family or work?	0	1	2	3	4
4. Do you feel embarrassed over your relative's behaviour?	0	1	2	3	4
5. Do you feel angry when you are around your relative?	0	1	2	3	4
6. Do you feel that your relative currently affects our relationships with other family members or friends in a negative way?	0	1	2	3	4
7. Are you afraid what the future holds for your relative?	0	1	2	3	4
8. Do you feel your relative is dependent on you?	0	1	2	3	4
9. Do you feel strained when you are around your relative?	0	1	2	3	4
10. Do you feel your health has suffered because of your involvement with your relative?	0	1	2	3	4
11. Do you feel that you don't have as much privacy as you would like because of your relative?	0	1	2	3	4
12. Do you feel that your social life has suffered because you are caring for your relative?	0	1	2	3	4
13. Do you feel uncomfortable about having friends over because of your relative?	0	1	2	3	4

14. Do you feel that your relative seems to expect you to take care of him/her as if you were the only one he/she could depend on?	0	1	2	3	4
15. Do you feel that you don't have enough money to take care of your relative in addition to the rest of your expenses?	0	1	2	3	4
16. Do you feel that you will be unable to take care of your relative much longer?	0	1	2	3	4
17. Do you feel you have lost control of your life since your relative's illness?	0	1	2	3	4
18. Do you wish you could leave the care of your relative to someone else?	0	1	2	3	4
19. Do you feel uncertain about what to do about your relative?	0	1	2	3	4
20. Do you feel you should be doing more for your relative?	0	1	2	3	4
21. Do you feel you could do a better job in caring for your relative?	0	1	2	3	4
22. Overall, how burdened do you feel in caring for your relative?	0	1	2	3	4
Total Score (out of 88)					

C-2 The Brief COPE

Brief Coping Orientations for Problems Experienced (COPE).

These items deal with ways you've been coping with supporting someone with Parkinson's disease. There are many ways to try to deal with this role. These items ask what you've been doing to cope with your situation. Obviously, people deal with things in different ways, but I'm interested in how you've tried to deal with it. Each item says something about a particular way of coping. I want to know to what extent you've been doing what the item says: How much or how frequently. Don't answer on the basis of whether it seems to be working or not—just whether or not you're doing it. Use these response choices. Try to rate each item separately in your mind from the others. Make your answers as true FOR YOU as you can.

1 = I haven't been doing this at all
2 = I've been doing this a little bit
3= I've been doing this a medium amount
4= I've been doing this a lot

	1	2	3	4
1. I've been turning to work or other activities to take my mind off things				
2. I've been concentrating my efforts on doing something about the situation I'm in				
3. I've been saying to myself "this isn't real."				
4. I've been using alcohol or other drugs to make myself feel better				
5. I've been getting emotional support from others				
6. I've been giving up trying to deal with it				
7. I've been taking action to try to make the situation better				
8. I've been refusing to believe that it has happened				
9. I've been saying things to let my unpleasant feelings escape				
10. I've been getting help and advice from other people				
11. I've been using alcohol or other drugs to help me get through it				
12. I've been trying to see it in a different light, to make it seem more positive				
13. I've been criticizing myself				
14. I've been trying to come up with a strategy about what to do				
15. I've been getting comfort and understanding from someone				
16. I've been giving up the attempt to cope				

1 = I haven't been doing this at all
2 = I've been doing this a little bit
3= I've been doing this a medium amount
4= I've been doing this a lot

	1	2	3	4
17. I've been looking for something good in what is happening				
18. I've been making jokes about it				
19. I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping, or shopping				
20. I've been accepting the reality of the fact that it has happened				
21. I've been expressing my negative feelings				
22. I've been trying to find comfort in my religion or spiritual beliefs				
23. I've been trying to get advice or help from other people about what to do				
24. I've been learning to live with it				
25. I've been thinking hard about what steps to take				
26. I've been blaming myself for things that happened				
27. I've been praying or meditating				
28. I've been making fun of the situation				

C-3 The Positive Aspects of Caregiving Scale

APPENDIX B
Positive Aspects of Caregiving

Some caregivers say that, despite all the difficulties involved in giving care to a family member with memory or health problems, good things have come out of their caregiving experience too. I'm going to go over a few of the good things reported by some caregivers. I would like you to tell me how much you agree or disagree with these statements. Please refer to the responses listed on this card. *[Give card to respondents.]*

Providing help to (CR) has . . .		*Disagree a Lot*	*Disagree a Little*	*Neither Agree nor Disagree*	*Agree a Little*	*Agree a Lot*	*Unknown*	*Refused*
4.1. (RC8)	Made me feel more useful	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	–3 ( )	–4 ( )
4.2 (RC8)	Made me feel good about myself	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	–3 ( )	–4 ( )
4.3 (RC8)	Made me feel needed	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	–3 ( )	–4 ( )
4.4 (RC8)	Made me feel appreciated	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	-3 ( )	–4 ( )
4.5 (RC8)	Made me feel important	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	–3 ( )	–4 ( )
4.6 (RC8)	Made me feel strong and confident	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	–3 ( )	–4 ( )
4.7 (RC8)	Enabled me to appreciate life more	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	–3 ( )	–4 ( )
4.8 (RC8)	Enabled me to develop a more positive attitude toward life	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	–3 ( )	–4 ( )
4.9 (RC8)	Strengthened my relationships with others	1 ( )	2 ( )	3 ( )	4 ( )	5 ( )	–3 ( )	–4 ( )

C-4 The Geriatric Depression Scale

Older Person's Mood Scale (GDS): Brief 15-item version.

Present Qs verbally, circling answer but do not show participant.
Say, **"Please choose the best answer for how you have felt over the past week."**
If necessary, repeat the question; get clear Yes/No (more yes or more no).
(circle all responses; count bold)

1. Are you basically satisfied with your life? Yes **No**

2. Have you dropped many of your activities and interests? **Yes** No

3. Do you feel happy most of the time? Yes **No**

4. Do you prefer to stay at home rather than going out and doing new things? **Yes** No
If none of the above responses suggests depressive mood, STOP HERE.

If any bolded responses above (suggests depression) ask questions 5-15.

5. Do you feel that life is empty? **Yes** No

6. Do you often get bored? **Yes** No

7. Are you in good spirits most of the time? Yes **No**

8. Are you afraid that something bad is going to happen to you? **Yes** No

9. Do you often feel helpless? **Yes** No

10. Do you feel that you have more problems with memory than most? **Yes** No

11. Do you think it is wonderful to be alive? Yes **No**

12. Do you feel pretty worthless the way you are now? **Yes** No

13. Do you feel full of energy? Yes **No**

14. Do you feel that your situation is hopeless? **Yes** No

15. Do you think that most people are better off than you are? **Yes** No

CHECK: Was Q12 Yes or No (circle) GDS SCORE:

C-5 The Geriatric Anxiety Inventory

GAI-SF: Please answer the items according to how you've felt in <u>the last week</u>.

Tick the circle under **Agree** if you mostly agree that the item describes you.
Tick the circle under **Disagree** if you mostly disagree that the item describes you.

		Agree	Disagree
1	**I worry a lot of the time.**	O	O
2	**Little things bother me a lot.**	O	O
3	**I think of myself as a worrier.**	O	O
4	**I often feel nervous.**	O	O
5	**My own thoughts often make me anxious.**	O	O

As before, please answer the items according to how you've felt in <u>the last week</u>.

	Agree	Disagree
I find it difficult to make a decision.	O	O
I often feel jumpy.	O	O
I find it hard to relax.	O	O
I often cannot enjoy things because of my worries.	O	O
I often feel like I have butterflies in my stomach.	O	O
I can't help worrying about even trivial things.	O	O
I get an upset stomach due to my worrying.	O	O
I think of myself as a nervous person.	O	O
I always anticipate the worst will happen.	O	O
I often feel shaky inside.	O	O
I think that my worries interfere with my life.	O	O
My worries often overwhelm me.	O	O
I sometimes feel a great knot in my stomach.	O	O
I miss out on things because I worry too much.	O	O
I often feel upset.	O	O

6.4 Appendix D

Factor Analysis of the Brief COPE.

Non-metric Multidimensional Scaling (MDS) using Guttman's Smallest Space Analysis (SSA) was used to gain a visual impression of the structural patterns and item clusters in the data of the Brief COPE. The input matrix of item similarities was generated using a Euclidian distance coefficient (Barrett, Hogan, & Hogan, 2009) which is a Euclidean distance index expressed as a proportion of the maximum-possible distance between objects, given a fixed measurement range for every object. Similarity ranges from 0 (identical magnitudes) through to 1, which represent the maximum stress value of 0.09 for a 2 dimensional solution, which is considered satisfactory according to criteria set by Young (1985). The graphical representation of the double scaled Euclidian distance transformations confirmed that the Brief COPE data from the current sample were not unidimensional and identified that some items pairs were not homogenous (Figure 6-1).

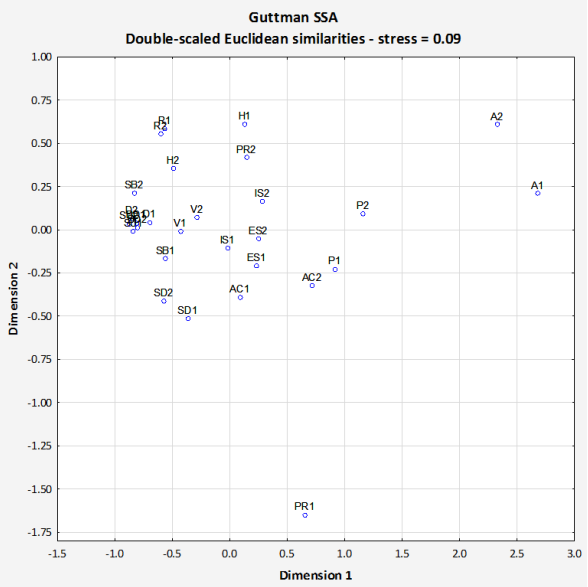

Figure 6-1. Non-metric MDS (SSA) solution for the subscale items of the Brief COPE questionnaire.

Following the SSA, principal components analyis with varimax rotation was undertaken to identify possible clusters among the individal items of the Brief COPE. The number of factors with eigenvalues greater than 1 (Kaiser, 1960) and the results of the scree test (Cattell, 1966) suggested that a 3 factor solution was optimal although previously published literature has used 9, 3 and 2 factor

solutions for the brief COPE (Carver, Scheier, & Weintraub, 1989; Cooper, Katona, Orrell, & Livingston, 2008; Snell, Siegert, Hay-Smith, & Surgenor).

In order to examine whether the current data could be rotated into maximal congruity with the previously published COPE target factor matrix (rather than solely to simple structure via the Varimax criterion), an orthogonal procrustes solution (Schonemann, 1968) was implemented using the Orthosim program (Barrett, 2006). This procedure transforms each matrix (the target and comparison matrix) to an orthogonalized form *(if both or either is an obliquely rotated matrix)* prior to rotating the orthogonalized comparison matrix to the orthogonalized target matrix, utilizing a least-squares criterion to establish the optimal fit between the two matrices. The procedure reports the 'target-comparison' fit as a series of conguruence coefficients between each respective component factor from both matrices. The procedure also reports a 'mean solution congruence' which is the average congruence computed across all Brief COPE items, where each target item vector (factor) is compared to its counterpart in the comparison matrix. An orthogonal procrustes solution presupposes an orthogonal target matrix; two previously published studies provided evidence that the Brief COPE was characterized by an orthogonal 3-factor solution (Coolidge, Segal, Hook, & Stewart, 2000; Cooper, Katona, Orrell, & Livingston, 2008)

The 3 factor solution for the brief COPE used as the target matrix describes problem-focused, emotion-focused and dysfunctional coping dimenstions (Coolidge, Segal, Hook, & Stewart, 2000; Cooper, Katona, Orrell, & Livingston, 2008). Comparisons were made between the target and the current data matrices to assess whether data from the current study was congruent with the target matrix. The congruence coeffiecnts between the targe matrix and the data from the curent study matrix roatated into maximal congruity via the procrustes procedure are shown in Table 6-1.

Table 6-1. Congruence coefficients and component-factor loadings from the maximally congruent orthogonal procrustes solution derived from a Principal Components factor analysis of the Brief COPE in a sample of PD patient caregivers (n=104).

	Factor 1 (Dysfunctional)	Factor 2 (Emotion-focused)	Factor 3 (Problem-focused)
Congruence coefficient	.76*	.67*	.84*
Self-Distraction 1	.62	-.06	.41
Self- Distraction 2	.51	-.06	.35
Denial 1	.25	.30	-.01
Denial 2	.32	.26	-.22
Substance Use 1	.64	-.35	.12
Substance Use 2	.60	-.17	.01
Behavioural Disengagement 1	.61	.06	-.08
Behavioural Disengagement 2	.55	.16	-.06
Venting 1	.56	.17	.22
Venting 2	.60	.44	.06
Self Blame 1	.37	.16	.20
Self Blame 2	.09	.25	-.04
Emotional Support 1	.18	.18	.69
Emotional Support 2	.12	.25	.64
Positive Reframing 1	-.02	.20	.31
Positive Reframing 2	.22	.64	.07
Humour 1	.05	.66	-.06
Humour 2	.14	.55	-.11
Acceptance 1	.03	.41	.22
Acceptance 2	.03	.59	.24
Religion 1	.21	.50	-.04
Religion 2	.21	.51	-.04
Active Coping1	.30	.10	.57
Active Coping2	.33	.22	.66
Instrumental Support1	-.06	.23	.74
Instrumental Support2	-.06	.54	.56
Planning 1	.23	.33	.52
Planning 2	.19	.52	.49

The recommended factor loading level of >.4 (Gorsuch, 1983) was achieved by all but the denial and self-blame subscales and one item from the positive reframing subscale. Items loading on to factor 1 included the self-distraction, substance use, behavioural disengagement and venting subscale items from the dysfunctional dimension. Items loading onto factor 2 included the religion, acceptance and humour subscales and one items from the positive reframing subscale which formed the emotion-focused dimension. The emotional support subscale loaded more strongly to items from factor 3, the problem-focused subscale. It was felt that seeking emotional support could sit well in a dimension associated with finding solutions, therefore it remained in that dimension along with active coping,

seeking instrumental support and planning subscale items. The overall solution congruence of .79 fell only just below the acceptable criterion of.8 (Streiner, 2003). The congruence coefficients between the corresponding target and input matrix component fators are provided in the first row of Figure 6-1 and are slightly below the preferred criterion but were also considered acceptable for research purposes (Streiner, 2003).

Internal Consistency

The Cronbach coefficient α was calculated for each of Carver's original subscale item pairings. All items pairs except positive reframing (.21) and denial (.49) exceeded Carver's criterion of .5, although self-blame(.57) and behavioural disengagement (.56) failed to reach the conventionally accepted criterion of .7 (Streiner, 2003).

1. Active Coping	α = .76	• I've been concentrating my efforts on doing something about the situation I'm in. • I've been taking action to try to make the situation better.
2. Emotional Support	α = .81	• I've been getting emotional support from others. • I've been getting comfort and understanding from someone.
3. Instrumental Support	α = .76	• I've been getting help and advice from other people. • I've been trying to get advice or help from other people about what to do.
4. Planning	α = .70	• I've been trying to come up with a strategy about what to do. • I've been thinking hard about what steps to take.
5. Humour	α= .79	• I've been making jokes about it. • I've been making fun of the situation.
6. Venting	α = .72	• I've been saying things to let my unpleasant feelings escape. • I've been expressing my negative feelings.
7. Acceptance	α = .70	• I've been accepting the reality of the fact that it has happened. • I've been learning to live with it.
8. Positive Reframing	α= .21	• I've been trying to see it in a different light, to make it seem more positive. • I've been looking for something good in what is happening.
9. Religion	α= .89	• I've been trying to find comfort in my religion or spiritual beliefs. • I've been praying or meditating.
10. Substance Use	α= .76	• I've been using alcohol or other drugs to help me get through it. • I've been using alcohol or other drugs to help me get through it.
11. Behavioural Disengagement	α= .56	• I've been giving up trying to deal with it. • I've been giving up the attempt to cope
12. Denial	α = .49	• I've been saying to myself "this isn't real". • I've been refusing to believe that it has happened.
13. Self-Blame	α = .57	• I've been criticizing myself. • I've been blaming myself for things that happened.
14. Self-Distraction	α = .84	• I've been turning to work or other activities to take my mind off things. • I've been doing something to think about it less, such as going to movies, watching TV, reading, daydreaming, sleeping or shopping.